CAPILLARY RESISTANCE STUDIES

IN

THE NEWBORN INFANT

AND IN

LATE PREGNANCY, LABOUR AND EARLY PUERPERIUM

BY

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SECTION I

CAPILLARY STUDIES IN THE NEWBORN

INTRODUCTION

Much valuable information has been accumulating during the 45 years since Hecht (1907) described his method of measuring capillary strength. Attention was drawn to the altered capillary function in scurvy by Hess and Fish (1914) and since that time the capillary resistance in many other diseases has been studied. Gothlin (1933), for example, found the resistance to be low in patients with albuminuria, but normal in cases of gastric ulcer and afebrile tuberculosis. Elliot (1938) discussed the changes in capillary resistance in cases of idiopathic thrombocytopenic purpura and reported the effect of splenectomy on the resistance. Griffith (1944) reported capillary tests in cases of hypertension, as did Shanno (1946) who also included examples of haemorrhage and drug reaction. Brown (1947) listed 20 conditions in which the capillary strength was reported to be low and presented his findings on examination of 60 cases. Munro, Lazarus and Bell (1947) reviewed the subject in relation to Vitamin C and

Vitamin P deficiency in man and gave a summary of capillary function relative to age, menstruation and seasonal variation. More recently Scar-:borough and Bacharach (1949) discussed in detail the relationship of Vitamin P and Vitamin C to scurvy, particular attention being paid to the capillary resistance; and Robson and Duthie (1950) described the effects of adrenocorticotrophic hormone (A.C.T.H.) on capillary resistance.

Paediatric interest in this subject has largely been related to the haemorrhagic lesions found in the newborn period, particularly those responsible for stillbirth and neonatal death. Though much experimental work was done on adults before 1920 it was only about this time that Ylppö did his original work with infants. In-:terest was rather lost in capillary resistance when Dam about 1935, after several years' work, established the existence of an anti-haemorrhagic vitamin and thus stimulated research into the treatment of hypoprothrombinaemic haemorrhage with Vitamin K. When it became obvious, however, that a certain number of cases of haemorrhagic disease of the newborn, hitherto regarded as hypoprothrombinaemic, did not respond to Vitamin K, workers began to search elsewhere for an explanation.

Bayer (1930), Lindquist (1937), Maloney (1943), Kerpel-Fronius et al (1948), and Minkow-:ski and Venes (1948) have done further work on capillary function in the search for the answer and have continued largely along the lines sugg-:ested by Ylppö (1924). With the high in-:cidence of haemorrhagic disease of the newborn in mind, and with the suggestion that this might be related to capillary resistance (Krepel-Fronius et al, 1948) further study of this subject seemed to be indicated.

REVIEW OF METHODS AND SOURCES OF ERROR

Negative and positive pressure tests: Munro et al (1947) reviewed the various methods by which the strength of capillaries have been estimated since Hecht's (1907) original work. The methods are divided into negative and positive pressure tests and it is well recognised that the results of these two methods on the one individual and in the same area of the body differ (Dieckmann et al, 1949). Although the positive pressure methods, such as the Hess, Rumple-Leede and Gothlin tests, have been more often employed than the negative pressure tests, an ever-increasing number of

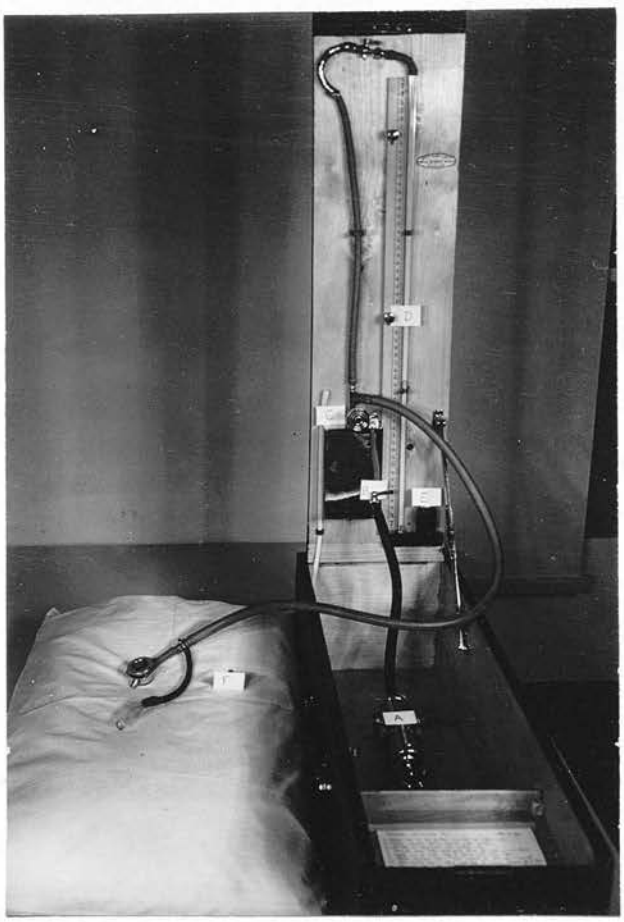


PLATE I.

workers have been using the latter since about 1930. A comprehensive list of these authors is given by Robson and Duthie (1950). It was decided to use a modification of the Dalldorf (1933) negative pressure test as described below, because it presented the least difficulty in standardisation, particularly when working with infants, and thereby allowed of a greater accur-:acy in the results. The apparatus employed was a slight modification of that used by Scarborough (1941). Plate I shows a hand-suction pump (A) which is used to evacuate a vacuum reservoir (B). (C) is a fine adjustment valve by which the mer-:cury can be sucked into the manometer (D) from the mercury reservoir (E). The mercury can be drawn up to any given level and steadily maintain-:ed to an accuracy of plus or minus 10 mms. by means of the valve. Distal to the valve there is a side arm to which the suction cups (F) are attached. When the cup is applied to the skin, the pressure within it is, therefore, the same as that indicated by the manometer. Although the time of exposure of the skin to the negative pressure is usually stated, it has not been made clear by some authors whether the 30 or 60 seconds exposure includes or excludes the time

taken for the apparatus to attain that pressure. Rough laboratory tests showed that the time taken for a water tap apparatus as used by Ylppö (1924) to reach a given pressure was much longer than the mercury manometer method used in the present experiments, and this author states the necessity of reaching a given pressure within a definite time.

Area tested: Writers are agreed that results can be compared only if the tests are made on the same area of the body. The skin reaction to negative pressure differs according to the site chosen and Wiemer (1931) gave average figures for various areas of the body surface. Bell et al (1940 and 1942) found a low correlation between the results on various parts of the arm. In the adult, some of the earlier workers used the "outer aspect of the arm", but the volar aspect of the forearm is now usually used; in the infant, no standard area has yet been established. Lindquist (1937) examined a number of infants, aged one to seven days, at a given pressure (400 mm.Hg.). He tested two areas in each case and found the percentage positive on the thorax significantly higher than on the leg. In 1935 he correlated the findings in various areas of the

trunk and limbs. Bayer (1930) tested the infra-clavicular region first and if a negative result was obtained, he then tested the sub-scapular region on the back. Kugelmass (1940) states that the resistance is minimum over the head and maxi-:mum in the extremities. Maloney (1943) used the Dalldorf method with 30 seconds exposure, but he does not mention the area tested. Ylppö (1924) and Minkowski and Venes (1948) used the dorsal region with a negative pressure method. It has been suggested by Gothlin (1937) and Roberts et al (1937) that greater accuracy could be obtained by testing both sides of the body and calculating an average. This is because Gedda (1931), for example, showed that the result on one arm differs on occasion from that on the other arm, and Greene (1934) found the left arm to show more positive results than the right.

Size of suction cup: Lindquist (1937) quotes Weimer (1931) as stating that the size of the suction cup and the suction dome of skin (up to 9 m.m. in height) are of no importance in the assessment of results. He quotes Frontali (1922) as having proved the latter point by preventing "doming" with a firm wire grid over the mouth of the cup. The results obtained with and without the

grid were the same. Bayer (1930) tried to limit the "doming" with gentle finger traction on the skin while suction was applied.

Maloney (1943) commented on the discrepancy between his own and previous reports, but offered no solution. It was noted that the figures quoted in these reports varied considerably. Abt et al (1936) used a cup with an internal diameter of ½ cm. Maloney (1943) and Dalldorf (1933) used a cup with a 1 cm. diameter, Ylppö (1924) and Borbely (1930) a 2 cm. diameter, and Lindquist (1937) used both and found no great difference between them. He did find, however, that with the larger cup there was a tendency to get more posi-:tive reactions at any given pressure. Dalldorf (1933) quotes most early workers, e.g. da Silva-Mello (1929)as having used a larger (3.5 cm.) cup. It seemed advisable, therefore, to re-investigate the effect the size of the cup had on the results (see below).

Skin texture: Lindquist (1937), Dalldorf (1933), Bell et al (1942) and Borbély (1930) are of the opinion that the skin texture and thickness are of importance. Differences in skin texture are hard to assess and classify and it was con-:sidered unnecessary in this investigation to

attempt this sub-division of cases. The diffi-:culty of the skin texture varying in different parts of the body was surmounted by performing all the tests in the same area. Desquamation, how-:ever, did make the reading of results difficult on occasion and the difference between petechiae and the red spot produced by the removal of a small scale of skin had to be learned.

Critical petechial pressure: The strength of a capillary is estimated by the production of petechiae and some workers, Brewer (1938) and Minkowski and Venes (1948) did not consider the test positive on the production of one petechia unless two or more were produced at a pressure 50 mm. higher. In the adults, the "critical petechial pressure" is described by Robson and Duthie (1950) as "that negative pressure, which when applied for 30 seconds, produces one or two petechiae only in the test area". If more than 10 petechiae were produced the test was repeated at a pressure of 50 mm.Hg. lower. Many authors define their own criteria of positivity of which to examples are quoted. This information is obviously of importance if the results (in terms of numbers of cases positive) of two different series are to be compared. It can readily be

appreciated that confusion may have arisen in the past if two series of tests, with different definitions of positivity, have been compared.

Bruising and oedema: A bluish discolora-:tion resembling a bruise is mentioned by Bayer (1930) who noted it in 7 out of 22 cases. He found no relation between this finding and the infants' weight, but noted that it was most often produced on testing the thighs. He also reported a deeper bruise on a single occasion. Lindquist (1937) considered the production of oedema important only in so far as it restricted the circulation and thus reduced petechial formation. Maloney (1943) notes that at high pressures he obtained free bleeding into the skin and finally Ylppö (1924) and Abt et al (1936) stated that they sometimes produced bruising and oedema. This discoloration made it difficult for Ylppö to count the petechiae and he postponed the estimation till the following day. As petechiae sometimes disappear within 24 hours this procedure has not been adopted. The relationship between the production of bruising and oedema and petechial formation seemed worthy of investigation and is discussed below.

Co-operation of the infant: A further source of error was noted during the present investigations. Though it was not mentioned by previous authoris it became obvious that a great-:er number of petechiae was produced at any given pressure when the infant was restless or crying than when it was lying quietly. A number of babies was tested while crying and while at rest, within a total time of an hour or two, e.g. before and after a feed, and the difference in the results was obvious. For this reason, certain tests had to be abandoned.

Time of testing: Robson and Duthie (1950) tested their adult patients at the same hour each day as there appears to be some change in capillary resistance within the course of a day, (Munro et al, 1947) and this may be related in some way to meals. As mentioned above, a lower figure was often obtained when the infant was at rest and it might be argued that the feed and not the fact that the child was restful is the im-:portant factor. It can be understood that it is wellnigh impossible - and probably unnecessary - to test all babies at the same time after feeds when large numbers of infants are being tested. Likewise, since the infants were born at any time

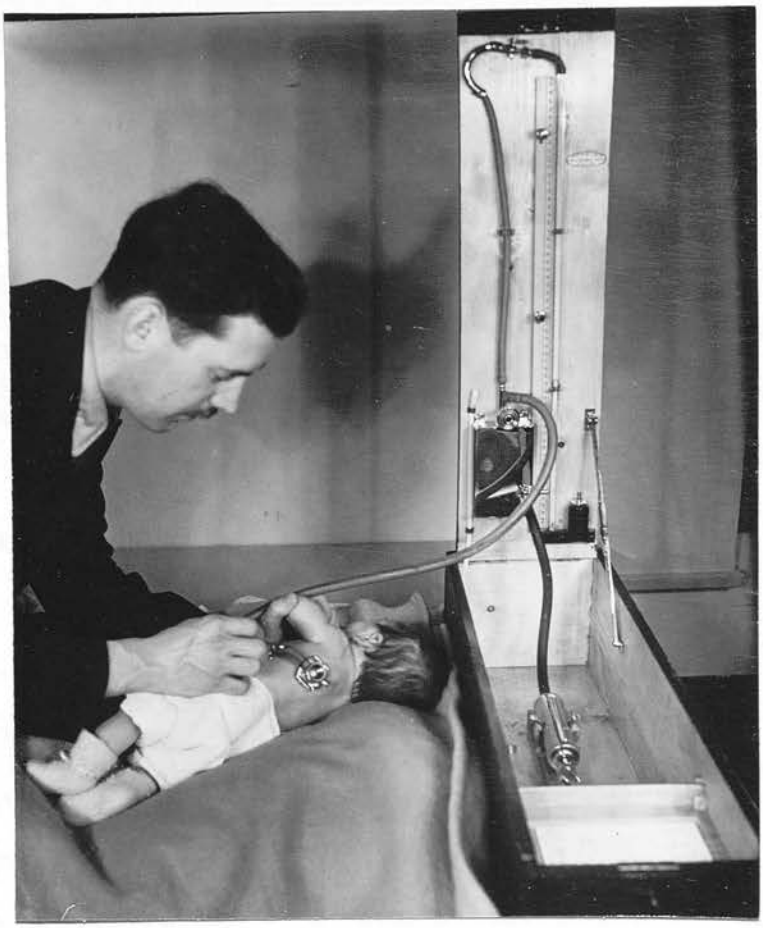


PLATE II.

PLATE III.

of day or night, the initial postnatal tests on mothers and the first infant tests had no fixed relation to the time of day or to meal times.

TECHNIQUE ADOPTED.

Throughout the present investigation, therefore, capillary resistance was measured with the negative pressure apparatus devised by Scarborough (1941) which is fully explained above. Certain modifications of the method used by previous workers were necessary. In the infants the estimations were made on the back, over the lower two-thirds of the thorax, (Plates II and III). Cups with internal diameters of 2 cm. and 1 cm. were used in the early stages of the work and the results were seen to be quite different. When it was found that the results obtained with these two cups could be correlated, the 1 cm. cup was discarded. A wire grid was not used. The procedure adopted by Bayer (1930) of limiting the "doming" within the cup by gentle finger traction was not adopted. It was con-:sidered impossible to standardise the traction as it would almost certainly vary from case to case and alter with the movement of the child

within the time of exposure. The negative pressure in all experiments was applied for 60 seconds (excluding the few seconds taken to reach that level) and the source of light was a 250-watt "photo flood" electric bulb. The importance of standardised lighting has been stressed by Bell et al (1940), and earlier by Molitch (1936) and Gothlin (1937), the last-named using a hand lens to examine the test area. The tested area was on each occasion examined through a hand lens for the first few months. Later, the lens was only used when there was some doubt about the positivity of the test. These modifica-:tions were necessary because the smaller petech-:iae in the infants were sometimes missed with the magnification and light of Scarborough's (1941) apparatus. The "critical petechial pressure"was estimated by raising or lowering the negative force by 50 mm.Hg. until a pressure which produced between 1 and 9 petechiae was reached. After an initial survey of about 50 cases, it was decided that the pressure producing 1 petechia only could be regarded as "critical", but a confirmatory negative result was always obtained with a pressure of 50 mm.Hg. lower. The infants were mature and free at the first testing from manifest infection or congenital

abnormality. A few premature cases are reported separately. In the early stages, infants of any age were tested, but latterly more attention was paid to those within the first week of life. The infants were tested in most cases when quiet and if very fractious, the test was abandoned for reasons given above. The cup was held firmly against the chest wall in order to give as air-tight a union as possible and it was seldom ne-:cessary to press very hard. The skin was examined for petechiae prior to testing and that number subtracted from the final result. No special time relation to meals was adhered to, though the in-:fants were more amenable after feeds and often slept throughout the test. If oedema was produced, it was allowed to disperse before the final petechial count was taken and a note was made of the presence or absence of a bluish discoloration over the while cup site.

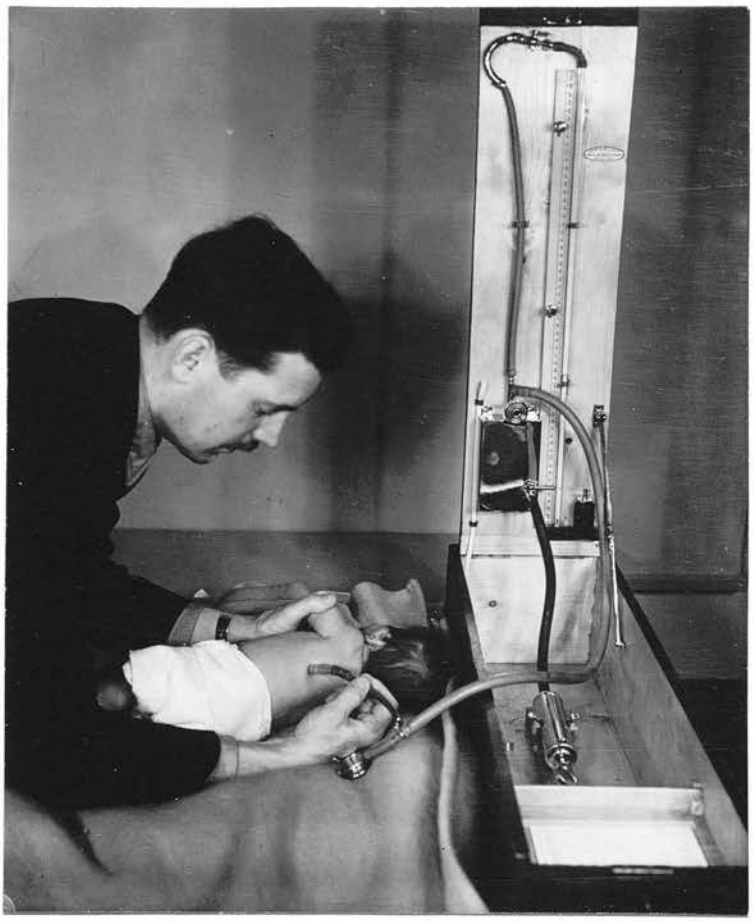


PLATE IV.

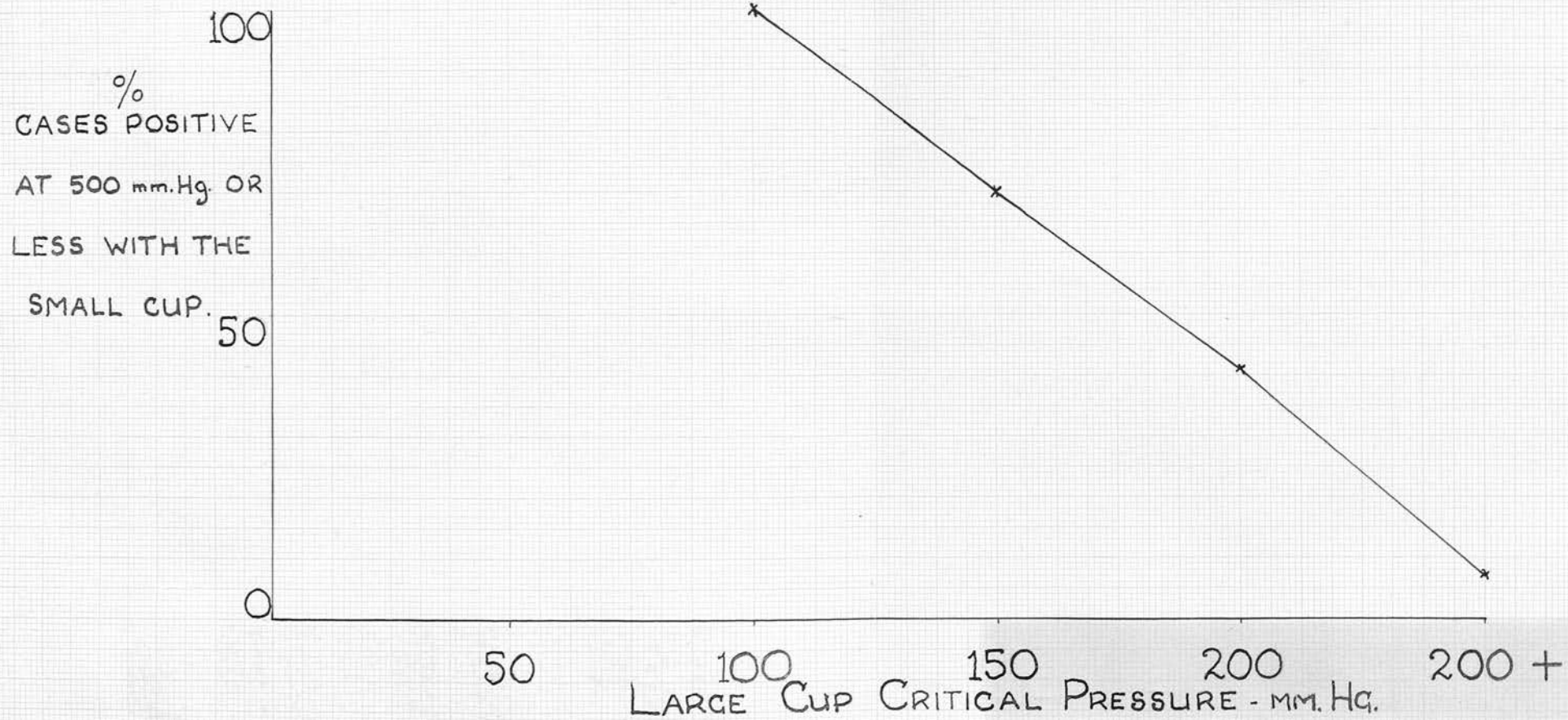
CHOICE OF CUP.

That there is some difference of opinion about the effect the size of the suction cup may have on the capillary tests has been mentioned above. A small experiment was, therefore, devised whereby the relationship between two cups could be ascertained. These had inner diameters of 2 cms. and 1 cm. respectively and 42 infants were tested with both in the manner described above; 67 estimations were made in all. The tests were performed as close together as possible in the dorsal area, and they were completed within about 5 minutes of one another. Plate IV shows the small cup in position.

TABLE I.

LARGE CUP READING mm. Hg.	SMALL CUP READINGS Nos of Positive Tests.								
	50	100	150	200	300	400	500	500+	TOTALS
50									
100		1		1	1		1		4
150				5	6	5	6	9	31
200							7	10	17
250							1	9	10
300								5	5
TOTAL									67

FIGURE I


100
%
CASES POSITIVE
AT 500 mm.Hg. OR
LESS WITH THE
SMALL CUP.
50
0
50
100
150
200
200 +
LARGE CUP CRITICAL PRESSURE - MM. Hg.

It can be seen (Table I) that a much higher pressure was required to obtain a positive result with the smaller cup. Figure I shows the close relationship between the results, the lower the critical level with the large cup, the more positive cases obtained at 500 mm.Hg. and less with the small one. Although the total number of tests is small the falling percentage relative to the large cup critical pressure is obvious; from 100% (4/4) positive with large cup readings of 100 mm.Hg. to 70% (22/31) at 150 mm.Hg., 41% (7/17) positive with large cup readings of 200 mm. Hg., and 7% (1/15) with readings of over 200 mm. Hg.

Many of the tests with the small cup read above 500 mm.Hg. (the maximum accurate reading of the apparatus) and seemed to produce discomfort.

As there appeared to be a close correlation between the cups and as the small cup required pressures high enough to produce discomfort, there seemed little to be gained by the use of the small one. It can be used, however, in the case of premature infants where the surface area available for testing is small, and where the critical level, even with the small cup, is well below 500 mm.Hg., i.e. below the levels apparently causing pain.

The large cup was, therefore, adopted for all further experiments on mature infants.

PLATE V.

BRUISING AND OEDEMA

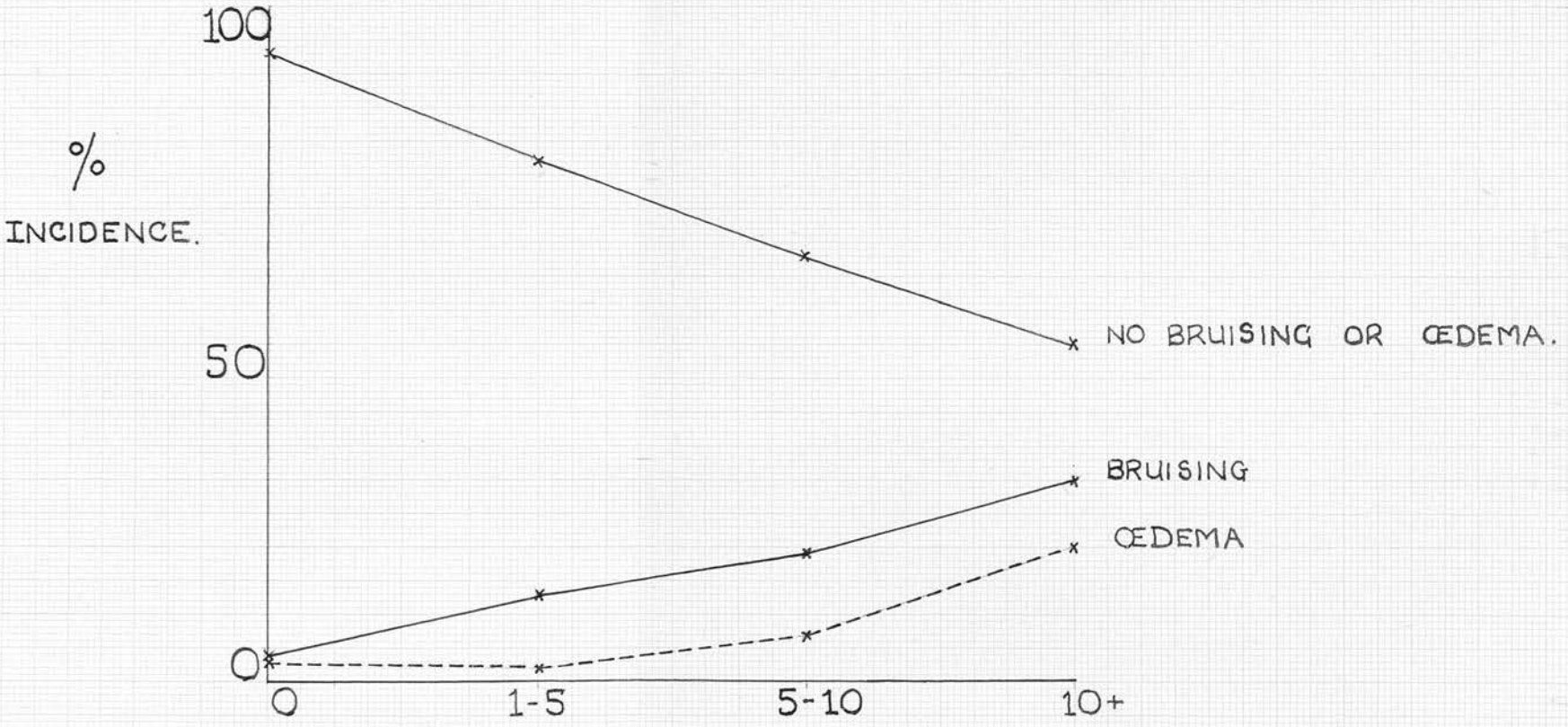
A brief review of the findings of several workers on the subject of bruising and oedema is given above. During the initial stages of this investigation these phenomena were encountered (Plate V) and latterly on 337 occasions a record of their presence or absence was made.

The findings were examined in an attempt to establish a relationship between the number of petechiae produced and the presence of bruising.

TABLE II.

No. of Petechiae Produced	Bruising		Oedema		Bruise and Oedema		Nil		Totals
	No	%	No	%	No	%	No	%	
0	5	4	3	3	-	-	106	93	114
1 - 5	22	13	3	2	14	8	131	77	170
5 - 10	8	19	3	7	5	11	27	63	43
10+	3	30	2	20	-	-	5	50	10

FIGURE II


100
%
INCIDENCE.
50
0
0
1-5
5-10
10+
NO BRUISING OR ŒDEMA.
BRUISING
ŒDEMA
NUMBERS OF PETECHIAE.

The tests were divided into four groups, those showing no petechiae, those showing 1 - 5, 5 - 10, and over 10 petechiae respectively, and the presence or absence of bruising and oedema was tabulated for each group.

On inspection of Table II and Figure II it can be seen that of the 114 cases showing no petechiae 106 (93%) showed neither bruising or oedema. Of 170 showing 1-5 petechiae, 131 (77%) showed neither. In the 5-10, and over 10 groups the figures were 27/43 (63%), and 5/10 (50%) respectively. Thus, an increase of bruising and/or oedema was noted as the number of petechiae increased.

No definite trend was noted in the percentage incidence of oedema alone. Experience showed that this oedema (which only occurs in infants) was of value in assessing results. It was not, as is suggested by Wiemer (1931), a complication which obscured the findings. There was a steady rise, however, in the incidence of bruising alone from 4% in the cases showing no petechiae to 30% in those showing over ten. Although this difference is not statistically significant due probably to there being only 10 cases in the second sample, the difference between the 4% and 19% (cases showing 5-10 petechiae) is significant.

Likewise examining the incidence of cases free from both oedema and bruising, the fall in

percentage from 93% in the cases showing no petechiae to 63% in those showing 5-10 petechiae is also statistically significant.

The exact nature of this discoloration is uncertain. No opportunity arose for examination of the skin lesion histologically. The fact that it could occur at all in the absence of petechiae rather indicates that it is due to a generalised dilatation of capillaries or, as suggested by Abt et al (1936), to transudation of blood into the extravascular space and not to punctate capillary rupture. Whether this find-:ing is an indication of capillary permeability rather than fragility is a point which must await further investigation. It can be concluded, how-:ever, that there is a definite relationship between bruising and the number of petechiae produced, i.e. the greater the number the more likely bruising is to occur. No such accurate relationship was shown in the case of oedema alone or of bruising and oedema occurring together, but it is possible that, given a greater number of cases in the "over ten petechiae" group, such a correlation might be obtained.

INVESTIGATION OF SEASONAL TRENDS IN INFANTS.

Most recent writers agree with two of the earlier workers, Gothlin (1931) and Gedda (1931) that in older children and adults the capillary resistance is low in spring and high in autumn. Roberts et al (1937) in the examination of 85 children, found April to be the month in which the resistance was lowest and August that in which it was highest. The age of these children was not given, but they were from a residential institu-:tion (were on a known diet) and are, therefore, not likely to be newborn infants. Brewer (1938) examining adult women, however, found a lower resistance in autumn than in the other seasons of the year. Brown (1947) on examination of 60 cas-:es gives winter and spring as the seasons in which the fragility was most marked. Munro et al (1947) are in partial agreement with Brown (1947) and state more precisely that spring and summer show the lowest resistance and winter and autumn show the highest. Kerpel-Fronius et al (1948) on examination of 233 children found the resistance greatest in the second six months of the year, March and April being the months showing the lower figures. Finally, it has been stated by Brown (1947), O'Hara and Hauck (1936) and in the case of children by Greene (1934) and Molitch (1935)

that the capillary resistance varies in the one person from time to time, though they do not detail all the factors, other than age and ill-:ness (Brown, 1947), that might cause these variations.

Kerpel Fronius et al (1948) reported a very close seasonal relationship between capillary resistance of young children and the incidence of certain haemorrhagic manifestations in the newborn. March and April were found to be the months in which fragility was greatest. No publications which confirmed these findings could be found.

There is some evidence that the incidence of stillborn infants shows a seasonal variation (Sutherland, (1949), Figure III). Earlier, Waddell and Lawson (1940) attempted to show a seasonal variation in neonatal deaths from intracranial haemorrhage, and suggested that hypoprothrombinaemia played a contributory part in the production of the haemorrhage. Their figures for the first 2 days of life, however, showed no such tendency, and the claim that Vitamin K might reduce deaths from intracranial haemorrhage are doubted. (Potter, 1952).

Kerpel Fronius et al (1948) in addition to the above also claimed that there was a definite seasonal incidence in cephalhaematoma and sub-:conjunctival haemorrhage in the newborn.

It seems relevant to mention the work of

Baye r (1931) on 49 cases showing some form of neonatal haemorrhagic disorder. He examined 13 cases of cephalhaematoma and found the capillary resistance lowered in eight of them. Hartley and Burnett (1944), on the other hand, do not mention capillary tests in their study of this condition and think that cephalamatomata occur in skull bones showing irregular ossification and that hypoprothrombinaemia may be an additional factor. Potter (1952), however, states that the underlying bone is "almost never abnormal".

Bayer (1931) also examined 9 cases of melaena and haematemesis and 14 babies showing petechiae at birth. All but one showed a low capillary resistance with or without thrombocytopenia.

During the present investigations, no cases of melaena or haematemesis were encountered. There were very few infants who showed petechiae at birth and the capillary tests on these yielded results so similar to the normal infants that the cases were treated as one group. So few cases of cephalhaematoma and subconjunctival haemorrhage occurred that no useful information could be ob-:tained by a separate analysis of the findings in these cases.

The seasonal incidence of cephalhaematoma over a two-year period was obtained from the infant case records of the Simpson Maternity Pavilion, Edinburgh. Although there is apparently a slight increase in the incidence in the months

May and June (Figure III) the trend is not very marked.

In the light of the above reports, two points presented themselves as being worthy of further research. Firstly, investigations were planned to see if there was a similar seasonal variation in the capillary resistance, not of the older infants as shown by Kerpel Fronius (1948) but of the newborn, and secondly, to find out if there was a parallel seasonal incidence of neonatal intra-:cranial haemorrhage in Edinburgh. (The city is stated advisedly as climatic (Brown and Wasson, 1941) and dietetic (see below) conditions vary markedly from place to place and many are of the opinion that capillary fragility is closely linked with these factors, the latter in particular.

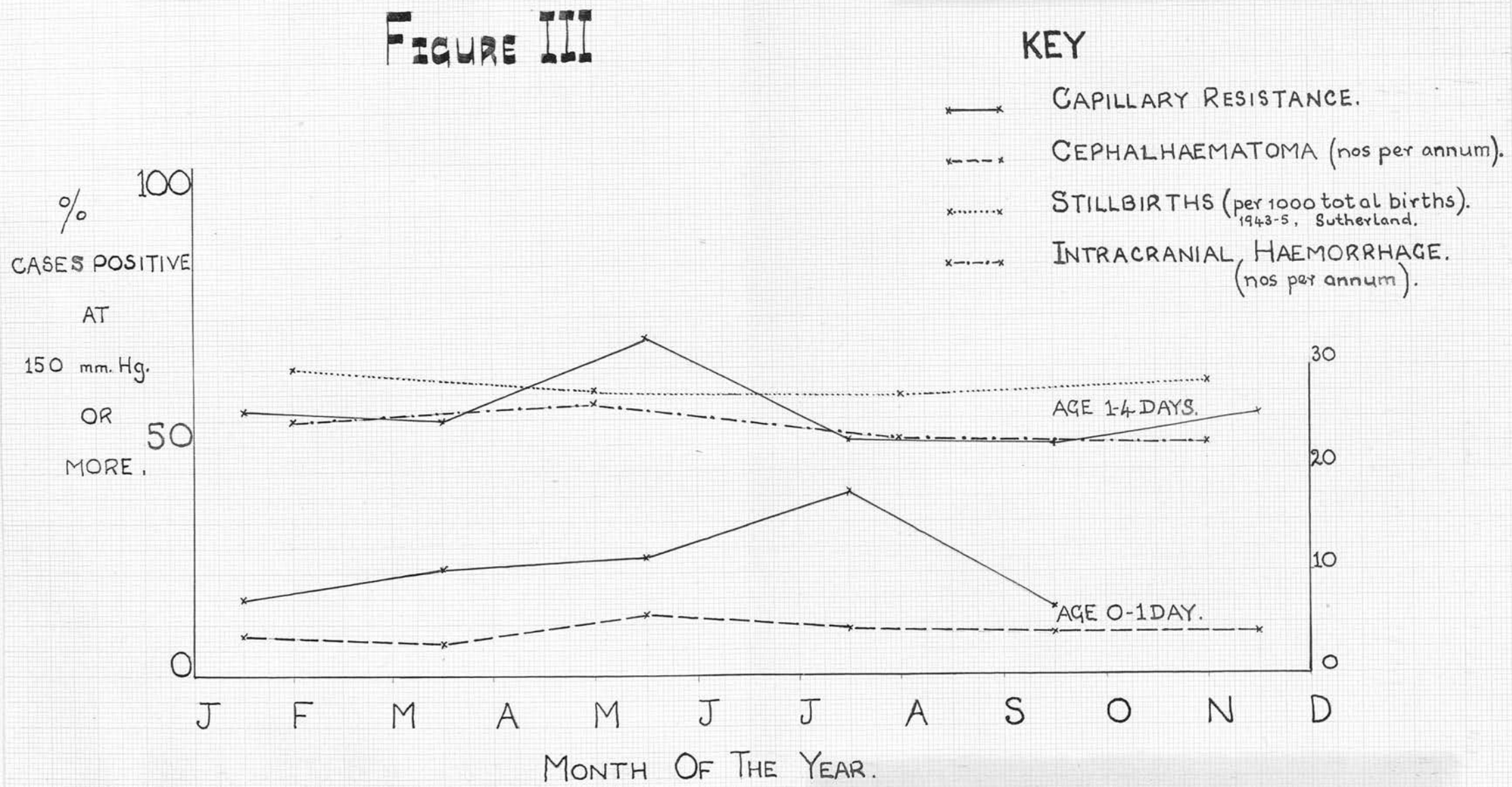
The investigations were performed over an 18-months' period, October 1949 to March 1951 inclusive, during which time 1,735 estimations of capillary resistance were made during 709 examinations of 518 newborn babies. The results obtained during the early months were discarded owing to possible inaccuracies while the technique was being perfected, thus 622 test results were used in the final analysis. It is regretted that while one of the workers was on holiday the other was unable to continue the investigations owing to pressure of routine work and no results for the month of August were obtained. Kerpel Fronius

TABLE III.

AGE	Under 24 Hours				1-4 Days				5 Days and Over			
Positive at mm. Hg.	100-		150+		100-		150+		100-		150+	
	No	%	No	%	No	%	No	%	No	%	No	%
JANUARY	8	80	2	20	18	34	35	66	0	0	15	100
FEBRUARY	9	90	1	10	33	63	19	37	4	36	9	64
MARCH	6	67	3	33	19	50	19	50	6	33	12	67
APRIL	12	92	1	8	16	50	16	50	3	33	6	67
MAY	21	72	8	28	15	43	20	57	6	23	20	77
JUNE	23	82	5	18	5	26	14	74	2	15	11	85
JULY	9	64	4	36	13	54	11	46	0	0	1	100
AUGUST	-	-	-	-	-	-	-	-	-	-	-	-
SEPTEMBER	22	88	3	12	7	54	6	46	-	-	-	-
OCTOBER	28	87	4	13	24	55	20	45	-	-	-	-
NOVEMBER	3	100	0	0	1	25	3	75	1	33	2	67
DECEMBER	14	100	0	0	14	64	8	36	1	50	1	50
Total	115	83	31	17	165	49	171	51	23	23	77	77

Seasonal trend and age analysis. 622 tests.

FIGURE III


KEY
CAPILLARY RESISTANCE.
CEPHALHAEMATOMA (nos per annum).
STILLBIRTHS (per 1000 total births).
1943-5, Sutherland.
INTRACRANIAL HAEMORRHAGE.
(nos per annum).
% CASES POSITIVE AT 150 mm. Hg. OR MORE.
100
50
0
30
20
10
0
AGE 1-4 DAYS.
AGE 0-1 DAY.
J F M A M J J A S O N D
MONTH OF THE YEAR.

et al (1948) considered pressures below 150 mm. Hg. to be low, but it became obvious that, when testing the normal newborn infant, figures of 50 mm.Hg. and 100 mm.Hg. were often obtained within 24 hours of birth. The apparatus was not accurate below 50 mm.Hg. and, therefore, no absolute figure could be quoted as being low. Experience showed that the best method of examining the results was to divide the cases into those positive (i.e. showing petechiae as described above) at 100 mm.Hg. or less, and those positive at 150 mm.Hg. or more. It was then possible to observe a trend in one or other direction. 622 test results are thus tabulated above (Table III) and it can be seen from these that there is no marked seasonal change in the capillary resistance in any of the age groups into which the cases have been divided.

Examination of the results in two monthly groups as done by Kerpel Fronius et al (1948) shows, in fact, an apparent rise in resistance in spring and summer, in the cases in which intracranial haemorrhage is most likely to be manifest - namely, those under 24 hours old. (Figure III and Table IV).

TABLE IV.

Seasonal trend of cases positive at 150 mm.Hg. or more.

	Aged Under 24 hrs	Aged 1-4 days	Aged Over 5 days
MONTHS	%	%	%
JAN - FEB	15	52	82
MAR - APR	21	50	67
MAY - JUN	23	66	81
JUL - AUG	36	46	-
SEP - OCT	13	45	-
NOV - DEC	-	51	58

The graph of the cases tested between the ages of one and four days of age does not show an identical curve, but again the tendency is for the resistance to be highest in the summer (Fig-:ure III). Statistical analysis of Table IV failed to show any significant seasonal variation and no trend could be detected by any re-arrangement of the monthly grouping. It would be unwise to draw any conclusions from this investigation, apart from the important fact that the newborn infant does not appear to have the same seasonal trends in capillary resistance as do older child-:ren or adults. Seasonal trends in capillary function appear then to be at the most only a contributory factor in the production of the minor seasonal variations in intracranial haem-

:orrhage in the newborn.

In order to investigate the second point the infant postmortem records of the Simpson Maternity Pavilion, Edinburgh, over an eight-year period, were examined. The quarterly variation in incidence of sub-dural, subarachnoid and intraventricular haemorrhage was tabulated. The pulmonary haemorrhage figures were obtained from the case notes over a three-year period.

TABLE V.

Seasonal Incidence of Neonatal Haemmorhage.

	Jan.- Mar. 1st	Apr.- Jun. 2nd	Jul.- Sep. 3rd	Oct.- Dec. 4th
Live Births	No	No	No	No
S.D.	38	28	31	33
S.A. + I.V.	62	81	86	77
Still births				
S.D.	49	36	39	42
S.A. + I.V.	19	30	6	8
P.H.	32	39	27	22
	First Half 71		Second Half 49	

Key: S.D. = sub-dural haemorrhage
S.A. = sub-arachnoid "
I.V. = intraventricular "
P.H. = pulmonary "

It can be seen from Table V that only the stillbirths with subarachnoid and intraventricular haemorrhage show a significant seasonal variation. There are many more cases in the second quarter than at other times, but this group only comprises 9% (63) of the total of 665 cases listed. It can be said, therefore, that no significant seasonal incidence in intracranial haemorrhage as a whole, such as described by Kerpel Fronius et al (1948) has been shown. In view of the findings in the previous section, it seems unlikely that capillary resistance and intracranial haemorrhage in the newborn have any close relationship. Even if the trends were fully significant, the months during which the resistance is low (the first and fourth quarter) do not correspond with those in which the intracranial haemorrhage is most evident(the second quarter). The seasonal trend in capillary resistance is compared with the seasonal incidence of intracranial and intrapulmonary haemorrhage, of stillbirths and of cephalhaematoma in Figure III.

One final observation should be made on studying Figure III. Bayer (1931) found that 8 out of 13 cases of cephalhaematoma had a low capillary resistance whereas in this investigation the months during which this lesion was found to be most common (May and June) are those in which the resistance is high.

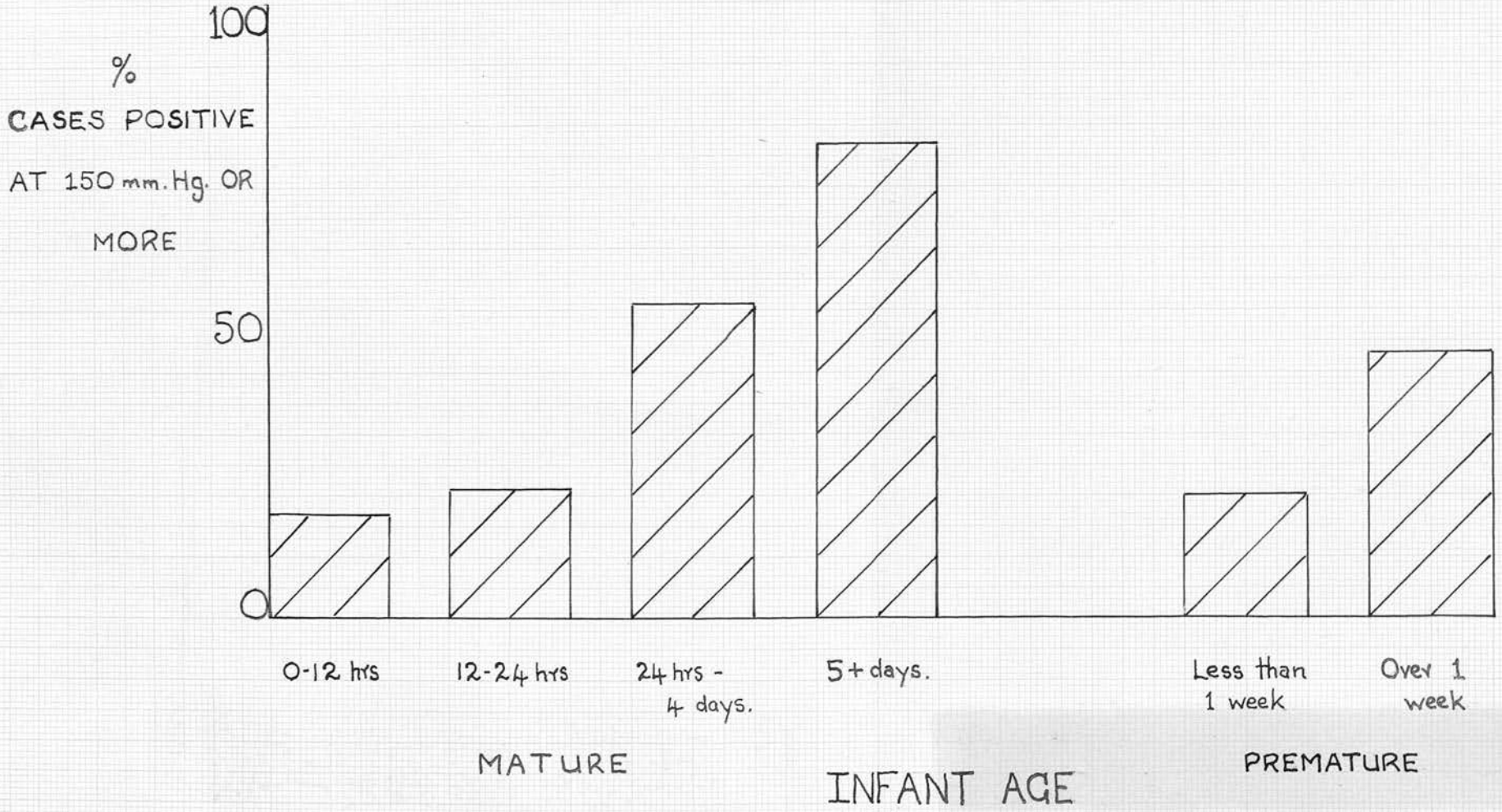
AGE TRENDS.

Bayer (1930) examined 52 cases, testing them all at a pressure of 220 mm.Hg. He found 52 to show petechiae at birth and none at the tenth day, concluding that a rise in capillary resistance during the first few days of life is a normal feature in full-term infants. Lindquist (1937) on the other hand, using a smaller cup (1 cm.) testing up to 500 mm.Hg., found no such trend over a 7-day period. Kugelmass (1940) stated that the resistance is high in infancy (500 mm.Hg.) gradually falling to the adult level of 150 mm.Hg. Clement Smith (1951) quotes Bernfeld (1931) as stating that the capillary resistance at "a few days" is high (600 mm.Hg.) gradually falling to adult levels (250 to 400 mm.Hg.) at the age of 2 years. No mention is made in the above of tests performed within the first few days of life, during which, according to Schwalm (1934), there is obvious histological development of the capill-:ary bed. Abt et al (1936) for example, state that the capillary resistance in the newborn is high, but did not test infants before the 3rd day of age. Munro et al (1947) found no Rumple-Leede response below 3 months of age and state that there is a decline in capillary resistance "with age". They quote Ylppö (1924), Bayer (1930) and Maloney (1943) all as stating that the

resistance rises in the first few days and grad-:ually declines till the age of two years. Dalldorf (1933) testing both adult s and children did not find any significant age trend, and Brown and Wasson (1941) found no such trend in children with rheumatism. The differing results in these reports could be caused by many factors, e.g. the inclusion of premature infants' results along with the mature, the use of negative or positive press-:ure methods, the size of the cup used, and the site chosen, and comparison of all these figures with the present series is not possible. Brock and Malcus (1934) found for example that in children capillary strength declined with age when the skin of the chest was tested, but it showed no such changes on the skin of the arm.

Thus, the age trends in capillary resistance under standard conditions seemed worthy of investigation, and 622 test results obtained from newborn infants examined during their 8 to 10 days' stay in hospital were analysed with this point in view. It soon became obvious that the pressure levels of tests done within the first 24 hours of life tended to be lower than those done after that time and that still higher press-:ures were required at and after the 5th day. The test results were, therefore, divided into three groups: - (1) those tested under 24 hours of age; (2) those between 24 hours and 4 days, and (3)

FIGURE IV


100
%
CASES POSITIVE
AT 150 mm. Hg. OR
MORE
50
0
0-12 hrs
12-24 hrs
24 hrs - 4 days.
5+ days.
Less than 1 week
Over 1 week
MATURE
PREMATURE
INFANT AGE

five days or more after birth. Table III shows the numbers of cases positive at 100 mm.Hg. or less and the numbers at 150 mm.Hg. or more at monthly inter-:vals. The percentages are also tabulated. As no significant seasonal variation was detected, a composite figure was obtained in each group (Table VI) and a diagram constructed (Figure IV).

TABLE VI.

AGE	Positive at 100 mm. Hg. or less		Positive at 150 mm. Hg. or more		TOTAL
	No	%	No	%	
Under 24 Hrs.	155	83	31	17	186
1 - 4 Days.	165	49	171	51	336
5 Days and Over	23	23	77	77	100
					622

Table VI shows that 83% (155/186) of infants under 24 hours of age had resistances of 100 mm.Hg. or less. 49% (165/336) aged 1-4 days, and only 23% (23/100) aged 5 days or more had positive tests at this level. This trend is statistically signi-:ficant.

It can be clearly seen that the younger the

infant the more fragile are the capillaries, at least within the age period covered.

Only a few premature infants were examined during these investigations, the results of which are presented separately in a later section. It is interesting to note that at this stage, however, Lindquist (1937) followed 7 premature infants for several months and found a gradual increase in resistance. A level corresponding to that found in a full-term mature infant was found when the infants were 2 to 3 months old, then a gradual decrease occurred. Examination of these premature infants' findings showed an average figure of 144 mm.Hg. in those tested under one week, and 200 mm.Hg. or more thereafter. No significant trend could be shown on examination of the cases in a similar manner to those presented in Table VI.

As the above result shows, the capillary resistance during the first 24 hours of life differs considerably from that at any other time in the neonatal period. 123 test results were analysed more critically to elicit any change in resistance that might occur within this 24-hour period. It is known that the resistance can alter markedly within the time of a surgical operation (Robson 1949, and Scarborough 1944) and the question arose as to whether the infant capillaries

respond to the factors initiating labour or to labour stress itself, and whether this response, if present, could be over within 24 hours of delivery. Accordingly, 111 of the 123 results were divided into 6-hour intervals and cases positive at 100 mm.Hg. or less tabulated separately from those positive at 150 mm.Hg. or more (Table VII).

TABLE VII.

Infant Age	0-6 Hrs.		7-12 Hrs.		13-18 Hrs.		19-24 Hrs.	
	No	%	No	%	No	%	No	%
Positive at 100 mm. Hg. or less.	30	86	26	78	18	90	18	79
Positive at 150 mm. Hg. or more	5	14	7	22	2	10	5	21

There appears to be (Table VII) a tendency for the capillary resistance to increase from birth onwards, though these results are in no way con-:clusive. 14% of 35 infants tested during the first six hours were positive at 150 mm.Hg. or more, whereas 21% of 23 tested between 19 and 24 hours were positive. Examination of these results in 12-hour intervals brings out the trend a little

more clearly (Table VIII and Figure IV). A further 12 results are added.

TABLE VIII.

Infant Age	0-12 Hrs.		13-24 Hrs.	
	No	%	No	%
Positive at 100 mm. Hg. or less.	62	83	38	79
Positive at 150 mm. Hg. or more.	13	17	10	21

In this instance, 17% of 75 cases tested in the first 12 hours were positive at 150 mm.Hg. or more and 21% of 48 tested in the 12 to 24 hour period were positive. Although this difference of 4% is not statistically significant, this result makes it very unlikely that there is an initially high capillary resistance at birth.

It is thus demonstrated that there was no initial high capillary resistance which could be missed if tests were not made within the first few hours of life. The infants had, as was suspected from previous findings, a low resistance at birth, which increased gradually during the neonatal period.

PREMATURITY.

Although prematurity is best defined in terms of crown-rump length, there are no universally accepted standards as yet. The more convenient method of assessing the infant's maturity by weight was used.

Bayer (1930), Ylppö (1924), Lindquist (1937) and Minkowski and Venes (1948) are all agreed that there is a relationship between the birth weight and the capillary resistance, the lower the weight the lower the resistance. Bernfeld (1931) gives the results of 36 infants under 2.5 K and concludes that there is no such relationship, but Lindquist (1937) re-examined the figures and found considerably more infants positive at the lower levels of pressure in the premature group. Sanna (1934) stated that the nail bed capillary in the premature resembled that of the mature infant on inspection and on testing with pressure changes, but added that the vessels tested were only the broader arches and not the finer loops which develop later. Eckstein (1933) reports that premature infant capillaries do not behave like mature vessels in respect of their response to heat and cold, and Schwalm (1934) describes the maturation of the former as seen through a capillary microscope.

He states that maturity is attained at about the fifth week in the skin of the chest wall. This does not entirely correlate with the age of two to three months given by Lindquist (1937) as the date when prematu re infants give a mature capill-:ary resistance result, but suggests there might be a connection between the histological changes observed and the response of the capillary to suction.

The 34 premature infants examined during this investigation showed a marked increase in fragil-:ity as compared with the mature infants. As very few premature infants could be tested within the first 24 hours of life and as they were only tested weekly, the results were divided into those obtained under and those over one week, and as before the percentage of cases positive at 100 mm. Hg. or less compared with those positive at 150 mm. Hg. or more. These results were tabulated against those obtained from mature infants between 24 hours and 4 days in the case of the premature babies below one week, and mature infants of 5 days or more in the case of premature babies over one week (Table IX).

TABLE IX.

	% Cases Positive at 100 mm. Hg. or less.		% Cases Positive at 150 mm. Hg. or more.	
AGE	Less than 1 week	Over 1 week	Less than 1 week	Over 1 week
PREMATURE	80	57	20	43
AGE	1-4 Days	5+ Days	1-4 Days	5+ Days
MATURE	49	23	51	77

At first glance it would appear that the 80% of premature cases positive at 100 mm.Hg. when tested during the first week approximates very closely with the 83% positive cases in full-term infants tested within 24 hours (see above). When it is remembered, however, that very few premature infants were tested within 24 hours of birth the 80% figure virtually represents cases tested between 1 and 7 days of age.

Table IX and Figure IV clearly show that the premature infant, like the mature, has an increase in resistance with advancing age. 20% of pre-:mature infants of less than one week old had a positive result at 150 mm.Hg., whereas 43% of infants over one week of age were positive.

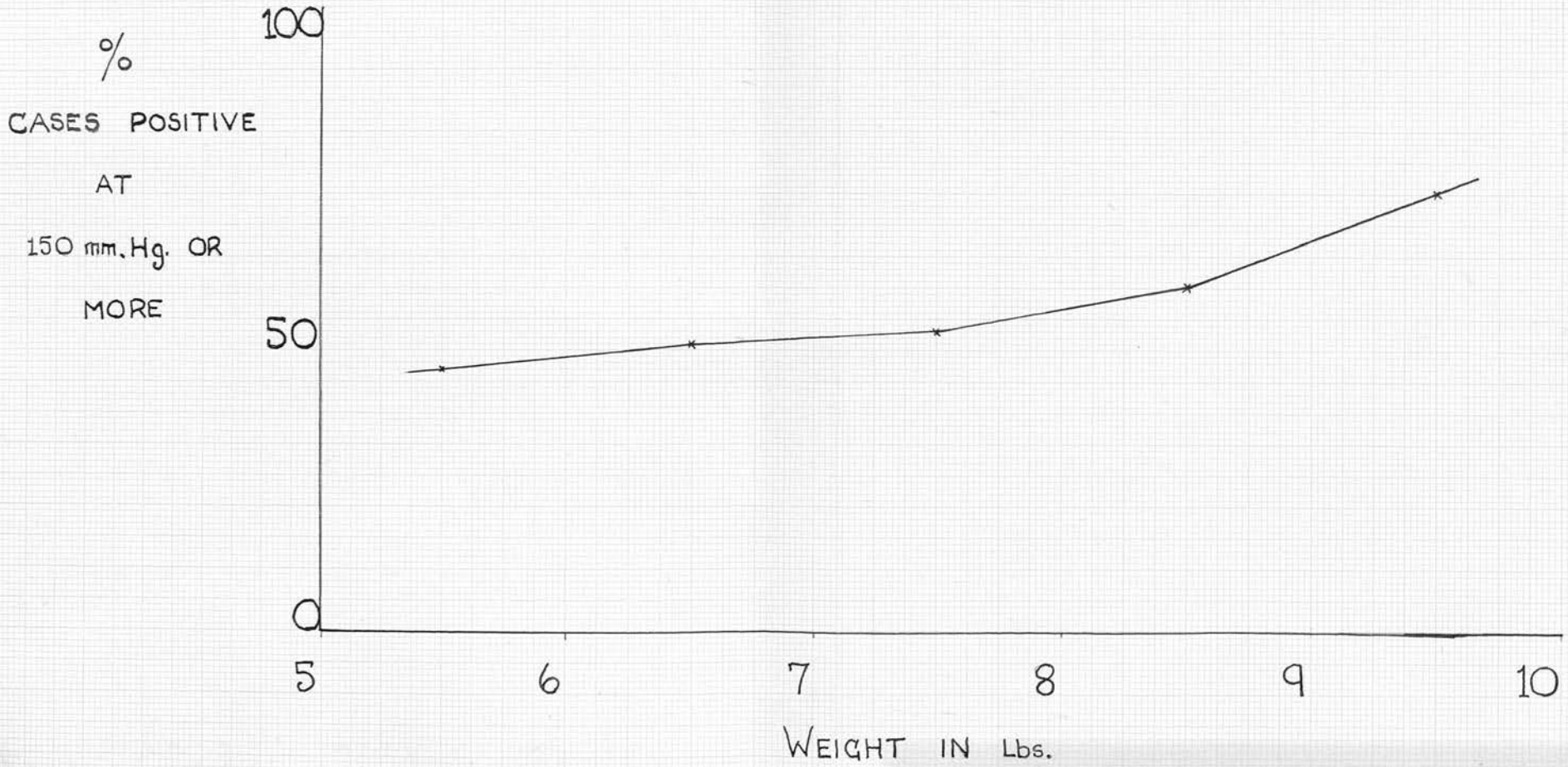
The difference between the mature and pre-:mature results in both age groups is statistically significant. It can be readily seen that many more

premature infants (80%) gave positive results at 100 mm.Hg. or less than did mature babies (49%).

Although this is a comparison of two groups not strictly comparable, it was considered, when the detailed timing of tests was examined, an interesting one worth making.

It was thus concluded that the premature, though less resistant initially, showed the same trend as the mature infants in respect of the increase in resistance with age. It was also noticed that the amount of brusing in premature infants was much greater and that it occurred without the appearance of petechiae on a number of occasions. This suggests that in these infants the suction was exerting its effect on a premature vascular bed in which the capillary, as seen in the older child, had not yet developed. The bruising was possibly caused by extravasation of blood into the tissues from a deeper vascular plexus.

FIGURE V


%
CASES POSITIVE
AT
150 mm. Hg. OR
MORE
100
50
0
5
6
7
8
9
10
WEIGHT IN Lbs.

THE EFFECT OF BIRTH WEIGHT ON CAPILLARY RESISTANCE IN MATURE INFANTS.

Lindquist (1937) examined 106 mature infants to see whether or not birth weight had any relation to capillary resistance. He concluded that there was no such relationship.

266 mature infants of this series were examined and the results tabulated (Table X). The cases were divided into 1 lb. weight groups starting at 5 lbs. This included a few premature infants between 5 lbs. and 5 lbs.8 ozs. for completion of the 5 lbs. to 5 lbs.15 ozs. group. All the infants were tested between the age of 24 and 72 hours, thus increasing the accuracy of the results.

TABLE X.

	5 - 5·15 lbs		6 - 6·15 lbs		7 - 7·15 lbs		8 - 8·15 lbs		9+ lbs	
	No	%	No	%	No	%	No	%	No	%
Positive at 100 mm.Hg. or less.	11	58	42	54	50	52	25	45	5	30
Positive at 150 mm.Hg. or more.	8	42	36	46	46	48	31	55	12	70
Totals	19		78		96		56		17	

Examination of Table X and Figure V shows that in this series of cases the direct relation-

:ship between resistance and birth weight (see above) is continued even within the mature group itself. 11 out of 19 cases (58%) in the 5 lbs. group were positive at 100 mm.Hg. or less and the remaining 8 (42%) at 150 mm.Hg. or more. The percentage of cases positive at the lower pressures gradually falls till the positions are reversed in the 9 lbs. and over group. In this instance, only 5 out of 17 cases (30%) were positive at the lower pressures, and although the numbers of cases at the extremes of weight are small, there are sufficient to indicate a significant trend. The probability of these changes occurring by chance is about one in twenty.

Thus, it appears that these conclusions do not in fact agree with those of Lindquist (1937). Re-examination of this author's figures shows a roughly similar trend, the significance of which is lost owing to a single result. This result cannot be overlooked, but it is not unreasonable to suggest that its effect might have been offset had there been a larger number of cases in the series.

SEX INCIDENCE.

Lindquist (1937) concluded from his series that there was no significant difference in the capillary resistance between the male and the female infant.

The results from 258 cases (137 males and 121 females) were examined and the percentage positive at various pressures tabulated. (Table XI).

These babies were all tested after 24 hours

and before 72 hours of age. Any variation in the results would, therefore, be due to a different response in the sexes and not to the fact that more of one or other sex happened to be within the period of maximum fragility (i.e. the first 24 hours). Examination of Table XI shows in fact no difference in the sex incidence.

In view of the findings in the previous section regarding the relationship between the

TABLE XI.

	Cases Positive at (mm. Hg.)								
	50		100		150		200		TOTAL
SEX	No	%	No	%	No	%	No	%	
Male	28	20	46	34	43	31	20	15	137
Female	19	16	43	36	38	31	21	17	121

resistance and birth weight, and in the knowledge that the female is not infrequently of lower birth weight than the male a difference between the sexes might have been expected. That this difference is not apparent is probably due to the fact that the capillary test is not sensitive enough to detect the small difference in resistance that might be present in two infants whose weight only varies by a few ounces.

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VITAMIN DEFICIENCY AND CAPILLARY RESISTANCE:

Since individuals suffering from certain pathological conditions have been shown to display abnormal capillary resistance, much work has been done in an attempt to account for these changes. Studies on normal children, (excluding infants) and adults showed seasonal incidence as discussed above and again efforts have been made to find a reason for these variations. The knowledge that the capillary resistance test was frequently positive in manifest and sub-clinical scurvy (Gyorgy (1927), Öhnell (1928), Gothlin (1931), Molitch (1936)) stimulated many later workers to investigate the effects of Vitamin C on capillary strength. Gianaroli, for example, as recently as 1945 noted that in war-time when there was a shortage of Vitamin C containing foods in Italy there was a reduction in the vitamin saturation in the body which had definite effects on capillary fragility. Although Bell et al (1940) found a significant rise in resistance on Vitamin C therapy when the initial resistance was low, they could not correlate the petechial count of their positive pressure method with the plasma vitamin C concentration. Abt et al (1936), with a negative pressure method, came to the same conclusions and Greene (1934) doubts whether this is a specific test of clinical or sub-clinical scurvy. O'Hara and Hauck (1936) found no

relationship between the capillary resistance and the urinary excretion of Vitamin C. Gothlin (1937) nevertheless was able to determine that a blood concentration of Vitamin C of 1 mgm per litre or less would effect a fall in capillary resist-:ance, and Dalldorf and Russell (1935) observed a prompt and prolonged rise in resistance follow-:ing intravenous ascorbic acid therapy. Several of the above authors attributed seasonal trends to changes in Vitamin C concentration. Brown (1947) makes the statement yet again that the capillary resistance is low in scurvy. Munro et al (1947) review the subject very thoroughly, and concluded that although there is a relationship between capillary resistance and Vitamin C it is not as close as the relationship between the resistance and Vitamin P.

There are those who still dispute the exist-:ence of a Vitamin P or substances with Vitamin P activity. Scarborough in 1939, however, presented a short history of Vitamin P and similar sub-:stances and produced good evidence (1939, and Scarborough and Bacharach, 1949) to support the idea that some factor other than Vitamin C had an effect on capillary fragility. Ten years after his early work, Scarborough, with Bacharach (1949) published a detailed account of the chemistry and pharmacology of Vitamin P and showed the relation-:ship between it and Vitamin C with particular

reference to capillary resistance.

Kugelmass(1940) thought Vitamin P was a flavone glucoside consisting of the two glucosides, Hesperidin and Eriodictyol. Scarborough and Bacharach (1949) suggest that there are several distinct compounds containing the active group which is present in Vitamin P. These compounds are mostly flavones, the most well-known being Hesperidin (a flavonone glucoside), Rutin (a flavanol) and Citrin (a concentrated extract of citrous peel). These authors state that the Citrin is the most active in Vitamin P activity, probably on account of its solubility. Scarbor-:ough (1945) gives the quantities of Vitamin P in Rose Hip Syrup, pure Hesperidin, and Citrin as 500, 100 and 650 units per 100 c.c. respective-:ly. Johnson in 1946 gave a detailed account of the pharmacology of Rutin, originally used therapeutically by Griffith (1943) and reported the results of clinical trials. Johnson (1946) enumerated several conditions in which this vitamin had been tried and had 88% (152 out of 173 cases) success in restoring the capillary resistance to normal. He also made the observa-:tion that the Vitamin C intake must be adequate, as this vitamin was apparently required to "activate" Vitamin P. Cotereau et al (1948) also discuss the relationship between Vitamins C and P. They suggest that Vitamin P is a Vitamine C sparing factor and that the latter cannot control

capillary resistance in the absence of this factor (Vitamin P) in the guinea-pig. Vitamin P alone had no marked effect on the resistance, but the administration of it reduced the body requirements of Vitamin C. Analysis of animal tissue showed that no storage of Vitamin C occurred in the ab-:sence of this sparing factor.

It is suggested by Parrot and Cot e reau (1949) that Para-aminobenzoic Acid may be normally concerned in the control of capillary resistance and that the resistance is raised by the limita-:tion of oxygenation of Vitamin C. It is also suggested that this limitation may be the method by which Vitamin P and Vitamin B exert their effect. Repeated giving of drugs of the sulphona-:mide group reduced the Vitamin C content of guinea-pig tissues.

Ambrose and De Eds (1947) support the view that Vitamin P on its own has no effect on the capillary function. They found Rutin had no effect on the high capillary permeability in scorbutic guinea-pigs, but that it did decrease permeability in rabbits. It is not stated that these rabbits were entirely healthy, but they were presumably not scorbutic. Raiman and Necheles (1947) testing mice in a negative pressure chamber found Rutin gave protection against the produc-:tion of pulmonary haemorrhages. They also found that propylene and ethylene glycol, ethyl alcohol and, to a less extent, glucose afforded some

protection.

Munro et al (1947) were not convinced that Vitamin P reduced the body's need of Vitamin C, but found that Vitamin P, though not apparently an essential to life, improved the capillary strength even when the diet was normal. They do mention, however, that scorbutic guinea-pigs which were not responding to Vitamin C alone, did so when Vitamin P was added to the diet. Finally, they suggest the mechanism by which these vitamins act is to prevent the oxidation of adrenaline. In scurvy, there is lack of collagen supporting tissue and vascular atonia. The vitamins delay the destruction of adrenaline, which in turn, increases capillary tone and diminishes the tendency to rupture.

Griffith et al (1944), Shanno (1946) and Kugelmass (1940) also report success in the treat-:ment of increased capillary fragility with Rutin. The first two authors had success in cases of adult hypertension, but this was not the experience of Schweppe et al (1948). Beaser et al (1944) found Vitamin P ineffective in cases of idiopathic thrombocytopenic purpura, rheumatoid arthritis and diabetes with lowered resistance.

Kugelmass (1940) made his observations of capillary resistance on children and found that Vitamin P had definite effects on cases of purpura of nutritional, allergic or infective origin. It had no effect on purpura of mechanical origin.

Only one other writer could be found who had examined children from this viewpoint. Minkowski and Venes (1948) gave Esculoside (a substance with Vitamin P activity) to two mothers at term. The infants showed a fall in capillary resistance which was unexplained. Seven premature infants given the vitaminshowed no significant change in capillary resistance.

It is obvious from the foregoing review of recent literature that Vitamins C and P are very closely related substances. Any naturally occurring deficiency state would probably include both vitamins and, for this reason, it was wonder-:ed whether both would require investigation during the present capillary studies.

Lund and Kimble (1943), whose work has been confirmed by Slobody et al (1947) investigated 94 babies and found that 21% had plasma Vitamin C levels below 1.0 mgms% and that 7% had levels below 0.6 mgms%. As 50% of the mothers had levels below 0.6 mgms%, they suggest that the placenta exerts a selective retention of Vitamin C, easily available to the foetus. Abt et al (1936) found mother and infant to have similar blood concen-:trations. As the mothers in the following investigation were all on approximately standard diets containing Vitamin C supplements and as it appears from the above that the foetus is assured of an adequate Vitamin C supply, it was decided to investigate the effects of Vitamin P alone on the

capillary resistance of newborn infants.

Finally, Scarborough and Bacharach (1949) made clear the important distinction between a scorbutic diet and a Vitamin P deficient diet. Animals given the latter were unaffected by Vitamin C and their purpuric tendency was altered by giving Vitamin P. They go as far as to say that the only worthwhile test of Vitamin P activity is the capillary one.

Investigation :

It was decided to see if Vitamin P, when given antenatally to the mother, had any effect on the capillary function of the infant at and after birth. 30 women were given 60 mgms. Vitamin P three times daily for at least the last four weeks of pregnancy. 27 others were taken as controls and were a strictly comparable group apart from the vitamin therapy. All the women were primi-:parous; at the onset of therapy they were entirely free from any form of complication of pregnancy, and both groups were given the same dietary regime. Capillary studies were made on the mothers before, during, and after labour, the results of which are reported in another section of this work. The vitamin was discontinued at term. The concentration built up in the maternal circulation would be maintained for about three days (Scarborough, 1945). After this time,

any fall in resistance could be due to withdrawal effects of the vitamin. Whether the infant would receive the vitamin in the breast-milk or not is unknown.

During the investigation, one mother in the Vitamin P group developed mild hypertension shortly before term; one had a discharging dental sinus, and one a septic polyp in the right ear. In the control group, one developed mild pre-eclamptic toxaemia, and one mild hypertension. The infants born of these mothers were, however, included in the calculations as the infants were clinically normal at birth, and it was considered that the effects, if any, of these conditions on the infants (and their capillaries) would be approximately the same in each group. One infant was stillborn in each group, leaving a total of 55 live babies.

TABLE XII.

AGE (days)	TOTALS		50 mm. Hg.				100 mm. Hg.				150 mm. Hg.				200+ mm. Hg.			
			P		C		P		C		P		C		P		C	
	P	C	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
1	25	22	7	28	9	41	14	56	7	32	3	12	3	14	1	4	3	14
2	7	10					3	43	5	50	2	28	3	30	2	28	2	20
3	7	14	1	14			1	14	6	43	5	72	7	50			1	7
4	14	9					3	21	3	33	5	36	2	22	6	43	4	45
5	9	6					3	33	1	17	4	45	4	66	2	22	1	17
6	3	12			1	8			6	50	1	33	2	17	2	66	3	25
7	11	8					1	9	2	25	5	45	3	37	5	45	3	37
8	6	9					1	17	2	22	4	66	5	56	1	17	2	22
9	1	1					1										1	
10	7	1					2	29			3	42	1		2	29		

Number of Tests positive at various pressures.

P = cases given Vitamin P

C = controls

Table XII shows the results of 182 tests on these 55 infants. The results are tabulated according to the pressure at which the test was positive and the age (in days) of the infant when tested. The results of the cases given Vitamin P are tabulated alongside the controls for purposes of comparison.

Examining the figures for the first 24 hours (the time at which the vitamin, if active at all, would exert its greatest effect) it is found that 28% (7/25) of the Vitamin P cases were positive at 50 mm.Hg. whereas 41% (9/22) of the controls were positive at this pressure. In the 100 mm.Hg. group 56% (14/25) of the Vitamin P cases were positive at this pressure and only 32% (7/22) of the controls. This suggests that the Vitamin P cases had in fact a greater resistance - fewer of them being positive at the lower pressure.

The tests made during the next three days show a similar trend, the combined percentage of the Vitamin P cases positive at 100 mm.Hg. being 25% (7/28) and the controls 42% (14/33). As before, the position in the next pressure group is reversed. 43% (12/28) of the Vitamin P cases were positive at 150 mm.Hg., whereas 36% (12/33) of the controls were positive at this pressure. This also suggests that more Vitamin P cases are in the higher pressure group, but no definite conclusion can be reached as these figures are not statis-:tically significant.

TABLE XIII.

	TOTALS P		TOTALS C		50 mm. Hg. P		50 mm. Hg. C		100 mm. Hg. P		100 mm. Hg. C		150 mm. Hg. P		150 mm. Hg. C		200+ mm. Hg. P		200+ mm. Hg. C	
	29		26		P		C		P		C		P		C		P		C	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Cases showing a RISE in Capillary Resistance	24	83	18	69	8	33	10	56	14	58	6	33	2	8	2	11				
Showing a FALL	3	10	5	19							1				2		3		2	
Showing NO CHANGE	2	7	3	12					1		2		1						1	

Variation from initial lowest positive reading.

P = cases given Vitamin P

C = controls

The results were next analysed from a different point of view and are displayed in Table XIII. The 55 cases were divided into Vitamin P and Control groups and tabulated according to the lowest positive pressure during the initial test (done during the first 24 hours) of each case. These were again sub-divided into cases which showed a subsequent rise, fall or showed no change in capillary resistance.

Several points are brought out in this Table: -

(a) that a higher percentage of Vitamin P cases 83% (24/29) showed a subsequent rise in capillary resistance than controls 69% (18/26).

(b) that more controls showed a subsequent fall than did Vitamin P cases, 19% (5/26) as opposed to 10% (3/29).

(c) that more controls than Vitamin P cases showed no change, 12% (3/26) as opposed to 7% (2/29).

(d) that the initial positive pressure was higher in the Vitamin P cases than in the controls. 52% (15/29) Vitamin P cases were positive at 100 mm.Hg. or more as opposed to 35% (9/26) controls, independent of the subsequent trend.

(e) that the cases showing no change or a fall subsequently had initial pressures of 100 mm. Hg. or more.

It would appear that Vitamin P has had some effect in strengthening the capillaries in these newborn infants, but unfortunately the numbers are small, and the possible trends are not statistically confirmed.

MODE OF DELIVERY.

No reference to the effects of instrumental delivery on capillary resistance could be found in the literature and it was considered worthwhile to put on record the results obtained during these investigations. 254 cases were analysed with this point in view and again for the sake of accuracy only tests made between 24 hours and 4 days of age were examined. Only 23 instrumental deliveries (B) were performed, leaving 231 spontaneous births (A). The cases were again divided into those showing critical pressures of 50, 100, 150 and 200 mm.Hg. respectively, and the percentages calculated. (Table XIV).

TABLE XIV.

CRITICAL PRESSURE mm. Hg.	50		100		150		200	
	No	%	No	%	No	%	No	%
A Spontaneous 231	37	16	81	35	79	34	34	15
B Instrumental 23	4	17	8	35	6	26	5	22

Although there is an apparent shift of cases in Group (B) from the 150 mm.Hg. to the 200 mm.Hg. group, the number of cases is so small that no

conclusion can be reached. Taking the cases in groups of 100 mm.Hg. or less and 150 mm.Hg. or more, there is no difference at all between groups (A) and (B).

From this analysis, it would appear that instrumental delivery is unlikely to effect capillary resistance. It should be remembered, however, that the tests were performed at least 24 hours after birth by which time the effects of such delivery on the resistance may have abated. The numbers of these group (B) tests performed between 1 and 4 days of age is so small that no conclusion can be reached. The number of results obtained within the first 24 hours is even smaller and an analysis of these was, therefore, consider-:ed to be of little value and was not made. It must also be borne in mind that almost all the cases in group (B) had Vitamin K and that its effect, if any, would be reflected in this analy-:sis.

Vitamin K. The subject of prophylactic Vitamin K therapy and its relation to hypopro-:thrombinaemic haemorrhage in the newborn has been adequately reviewed by Potter (1945). That haemorrhagic disease at this age is sometimes due to a factor or factors other than, or in addition to, Vitamin K has become widely recognised.

Some of the literature concerning the effects of Vitamin K on intracranial haemorrhage has been

quoted above. Very little, however, has been published concerning the effects of this vitamin on capillary resistance. In 252 cases it was noted, therefore, whether or not the infant received the vitamin and the capillary resistance in two groups was tabulated. It should be mentioned that the vitamin was given only when the infant was delivered instrumentally or showed signs of shock or cerebral irritation at birth.

TABLE XV.

	VITAMIN 'K'		CONTROLS	
Positive at	No	%	No	%
50 mm. Hg.	7	19	33	15
100 mm. Hg.	12	33	75	35
150 mm. Hg.	12	33	71	33
200+ mm. Hg.	5	16	37	17
	36		216	

Although it could be argued that any difference between the Vitamin K treated group and the controls might be due to the selective nature of the

former cases, it is clearly seen from Table XV that there is no demonstrable change in capillary resistance. It is possible that these cases might have shown capillary resistance changes had the vitamin not been given. It is more likely, however, that neither the effects of delivery per se nor the vitamin had any influence on the capillary fragility.

RELATIONSHIP OF CAPILLARY RESISTANCE TO PERIPHERAL CIRCULATION.

Close observation of an infant during the first few days of life reveals the considerable change in colour and temperature of the extremities that can occur within quite a short space of time. Within 24 hours of birth an infant may be warm and pink, warm with cyanosed limbs, or cold and cyanos-:ed, or pale - irrespective of the infant's cloth-:ing or the heating of the cot or nursery. Lind-:quist (1937) studied the subject of "Neonatal Erythema" which he states as being maximal at 24 to 48 hours after birth. He considers this colour change to be a response to the cold extra-uterine environment, but observed it in only 43 out of the 108 cases tested. He explains this low incidence by suggesting that the erythema had passed off before the initial examination. He compared the capillary resistance by observing the percentage of cases positive up to 500 mm.Hg. in the erythema cases and a control group of different ages and found no appreciable difference. Eckstein (1933), quoted by Smith (1951), studying the capillary function of the newborn found capillary contraction in a cold environment and dilatation in a warm one, but made no mention of cyanosis. He states incidentally that the cap-:illaries of premature infants do not respond so

rapidly to warmth as they do to cold.

The presence of peripheral cyanosis is indicative of anoxia, and this in the normal infant may be caused either by central anoxia, anaemia or peripheral circulatory stagnation. Henry et al (1947) state that oxygen saturations below 15% and possibly even 25% increase capillary permeability. They are of the opinion that anaemia is the most important factor. It is of interest to note that Scarborough (1939) is of the opinion that the haemoglobin level per se has no effect on capillary fragility. That capillary permeability and fragility are quite separate entities is stressed by Ambrose and De Eds (1947), but they also state that an increase or decrease in the one is roughly proportional to similar changes in the other. Bell et al (1942) could not demonstrate this relationship, however. It is of importance to note also that Clement Smith (1951) on examining 31 newborn infants found oxygen saturations below the 15 to 25% level on 20 out of 121 (16.5%) occasions. On the other hand, Hopps and Lewis (1947) found that anoxic anoxia in guinea-pigs did not influence capillary permeability to globulin, and suggest that positive results obtained when stagnant anoxia is present are due to carbon dioxide excess damaging the capillary and not to oxygen deficiency.

97 cases were, therefore, analysed to see if there was any relationship between capillary

resistance and peripheral circulation. The cases were divided accordingly into those showing cyanosis (26) and those not doing so (71).

TABLE XVI.

		CYANOTIC (26)				ACYANOTIC (71)			
Critical Pressure mm. Hg.		100 -		150 +		100 -		150 +	
A	No	16		10		49		22	
	%	62		38		69		31	
Critical Pressure mm. Hg.		50	100	150	200	50	100	150	200
B	No	11	5	6	4	28	21	16	6
	%	43	19	23	15	39	30	23	8

The top half of Table XVI shows the numbers and percentage of cases in each group showing critical pressures of 100 mm.Hg. or less and 150 mm.Hg. or more (A). The lower half (B) shows these results split into their component parts. Neither A nor B show any significant difference between the cyanotic and acyanotic groups.

An accurate estimation of skin temperature

was not made and an assessment of the results from this point of view was, therefore, not thought justifiable.

As the cyanosis in these normal infants is almost certainly due to stagnant anoxia, it can be concluded that this investigation shows the capillary resistance not to be influenced by anoxia of this severity and duration.

JAUNDICE

It is well recognised that petechiae are sometimes found in patients suffering from jaundice yet few references could be found describing the capillary resistance in jaundiced newborn infants. Lindquist (1937) states that he found no change in the capillary resistance of 11 icteric infants comparing their results with non-icteric controls, and Bayer (1930) having examined 160 newborn babies, also concluded that jaundice had no effect on capillary resistance.

One further sub-division of case results was, therefore, made. 256 infants were divided into two groups, (A) 79 who had obvious jaundice at or after the time of testing, and (B) 177 who never showed clinical icterus. This incidence of 31% is rather below that suggested by Ellis (1951) and Mitchell and Nelson (1947) who quote figures of over 50% and 50% to 75% respectively. This is probably due to some infants being tested on the second day developing jaundice late and being missed. All tests were again performed between 24 hours and 3 days of age.

TABLE XVII.

Critical Pressure mm. Hg.		50		100		150		200	
		No	%	No	%	No	%	No	%
A	Jaundice 79	16	21	30	38	23	29	10	12
B	No Jaundice 177	27	15	61	35	59	33	30	17

Although in Table XVII there appears to be a slightly higher percentage of cases positive at the lower pressures in Group A (i.e. those with jaundice) the difference is not statistically significant. These findings thus agree with those of previous workers in showing that jaundice does not influence capillary resistance in the newborn.

SECTION II.

CAPILLARY RESISTANCE IN PREGNANCY, LABOUR AND THE PUERPERIUM.

The details of technique and the reasons for adopting the particular method used during these investigations have been discussed above. One or two points of difference between the infant and adult tests and between the method chosen for these experiments and some used by other authors are worthy of reiteration.

The principal difference between the infant and adult tests w as the site chosen. In the adult, the volar aspect of the forearm was used and the medial aspect just distal to the elbow crease was first tested (Area "A"), (Plate VI). In the early stages the lateral aspect (Area "B"), and the area just proximal to the wrist joint (Area "C") were tested but later (particularly during labour) only Area "A" was used so that the patient was as little disturbed as possible. The time of each exposure was one minute and not 30 seconds as described by Brewer (1938), Scarborough (1941), Robson and Duthie (1950) and the critical pressure was as described by Robson and Duthie (1950), i.e. the pressure at which 1 to 10 petechiae were produced. No negative result 50 mm.Hg. lower was

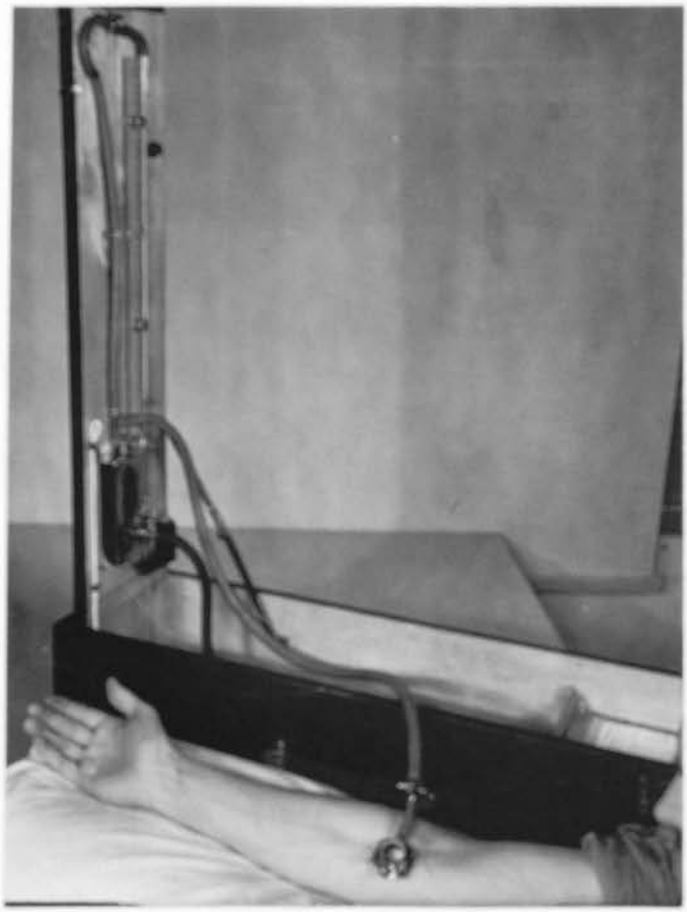


PLATE VI.

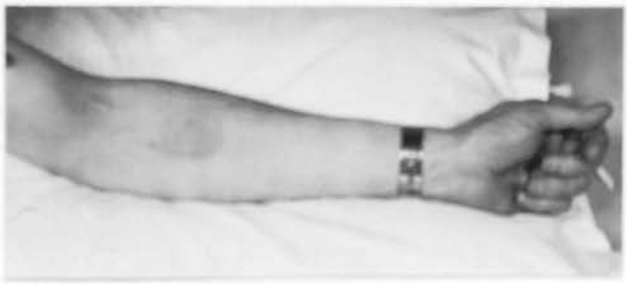


PLATE VII.

required. Robson and Duthie (1950) examined their cases at the same time of day in order to offset any diurnal variations. Munro et al (1947) also state the necessity of doing serial resistance tests at a fixed time of day owing to an apparent decrease in strength as the day advances. This was not possible in the present series on account of the varying time of birth of the infant. The initial post-partum reading was taken, therefore, at any time of day or night, but tests thereafter were usually performed between 10 a.m. and 12 noon. Plate VII shows a vigorous positive reaction in a central position on the forearm chosen specially for photographic reasons.

Apart from the antenatal and intrapartum tests most mothers had a test performed as soon after labour as was possible and thereafter two or more further tests were done at 2-day intervals according to the duration of stay in hospital.

NORMAL TRENDS IN CAPILLARY RESISTANCE IN THE ADULT

Before estimating the changes in capillary resistance over the period of childbirth, it is necessary to consider the variations that exist in the normal adult.

There is considerable disagreement as to whether or not age has an effect on capillary resistance and the subject has in part been reviewed in a previous section. Cutter and Marquardt (1930), Brown (1947) and Tey (1940) found a decrease in resistance with advancing age in adults, but Dalldorf (1933) found no such trend. In the adult, it has been found that one area of skin (the elbow) can show a change of capillary strength with age, whereas another (the wrist) does not (Munro et al, 1947). This finding might explain some of the variable results obtained by different workers, but as the camps are still divided, it was decided to limit the age of the mothers chosen for this experiment to between 20 and 30 years. It was considered that the change within a 10-year period, if present, would be too small to affect the results.

Seasonal variations have been reported by many authors and this factor was counteracted by performing all the maternal tests in the Vitamin "P" experiment and most of the non-pregnant con-

:trols (see below) within a period of 4 months. The vitamin treated and non-treated mothers were selected approximately alternatively so the two series ran parallel. The diurnal variations are mentioned above.

The question of menstruation does not enter the picture in the case of the pregnany mother, but it does with the non-pregnant controls. Brewer (1938) has studied the subject in detail and found, as did Bell et al (1940), a pre-menstrual drop in capillary resistance and quite a sudden fall just as the menstrual flow begins. Four days after the menses cease, the resistance has returned to normal. Stephan (1921) also observed changes during the menstrual cycle, and O'Hara and Hauck (1936) found inconclusive trends of the same nature as Bell et al (1940). Seventy-four volunteers were accepted at random from the nursing staffs of two hospitals and it was con-:sidered unnecessary to obtain details of the menstrual state of this number of controls.

THE EFFECTS OF NORMAL PREGNANCY, LABOUR AND PUERPERIUM ON CAPILLARY RESISTANCE.

McLennan (1946) and Browne (1944) have noted an increase in capillary permeability in later pregnancy.

Minkowski and Venes (1948) found the resist-:ance lowest at full dilatation of the cervix during labour, and also found, on examination of 37 women, that there was a slow post-partum rise in resistance reaching normal within a few weeks. Gianaroli (1945) also found the resistance to be lowered during pregnancy, especially towards term, and returning to normal within 3 months.

Dieckmann et al (1949) state the normal capillary resistance to be 200 to 250 mm.Hg. and examined 164 cases showing pregnancy hypertension or toxaemia by both negative and positive pressure tests. The results are mentioned below. Robson and Duthie (1950) give 250 to 350 mm.Hg. as the average range for their method which is similar to the one used in this experiment except for the method of lighting, magnification, and the time of exposure. These workers used a 30-seconds exposure in contrast to the 60-seconds in the present experiments. They also mention the wide variations in normal found by Bell et al (1942) ranging from 200 to 450 mm.Hg.

Roberts et al (1944) testing women during pregnancy found an abnormal increase in capillary pressure after histamine injection and increased cutaneous lymphatic flow, and found the actual capillary count to be normal in most cases. Browne (1944) found an increase in capillary pressure in later pregnancy in the lower limbs. Bean et al (1947 and 1949) report the observation of vascular spiders and palmar erythema from the second month of pregnancy, the spiders increasing in number till term. These were present in 65% of white women with uncomplicated pregnancies and disappeared mostly within the first week of the puerperium. Some spiders, however, were observed till about the 7th week after delivery.

It was decided, in view of these interesting observations, to analyse the maternal results and see if an ante-partum fall and post-partum rise in capillary resistance could be demonstrated. As Vitamin P has been shown to have no significant effect on maternal capillary resistance, the Vitamin P treated and the untreated cases were taken as one group to be compared with the non-pregnant controls.

74 non-pregnant controls were each tested on one occasion and the results dividend into (1) those positive at 150 mm.Hg. or less; (2) those positive at 200 mm.Hg., and (3) those at 250 mm.Hg. or more. Table XVIII shows the

detailed analysis of these results.

TABLE XVIII

NON PREGNANT CONTROLS	CRITICAL PRESSURE (mm. Hg)				
POSITIVE CASES	100-	150	200	250	300+
Nos	3	13	45	7	6
Nos	16		45	13	
%	21·6		61·4	17	

21.6% of the controls were positive at 150 mm.Hg. or less, 61.4% at 200 mm.Hg. and 17% at 250 mm.Hg. or more. These controls might be expected, when tested for 60 seconds, to have a lower average pressure reading than those tested for 30 seconds by other workers. This indeed is the case, the mean pressure being 200 ± 87 mm.Hg. (i.e. ± 2 x S.D.) S.E. of mean = 5.05 mm.Hg.

These results were compared with 174 Area "A" test results performed on 57 mothers during their last 6 weeks of pregnancy. As Vitamin P has no apparent effect on capillary resistance (see below) 30 mothers receiving this therapy were included. Their results were analysed in the same

way as the non-pregnant control findings (Table XVIII) and the composite Table XIX shows the comparison.

TABLE XIX.

Time Before Term (weeks)	CRITICAL PRESSURE (mm. Hg.)					
	100	150	200	250	300+	TOTALS
6 -		5	9	2		16
5 -	1	9	8	2		20
4 -	1	11	11	8	1	32
3 -	4	6	14	2	2	28
2 -	3	10	9	10	2	34
1 -	3	12	19	9	1	44
Nos	65		70	39		174
%	37·4		40·2	22·4		

During the week immediately before term, when the resistance is reputed to be at its lowest, 44 tests were made. The analysis of these 44 tests is shown in the composite Table XX in addition to the percentage positive tests in the three stated groups in one-week periods. The numbers in the 5th and 6th immediate ante-natal weeks

were too small to be of value.

TABLE XX.

AREA A	No	CRITICAL PRESSURE		
		150 mm.Hg. or less %	200 mm.Hg. %	250 mm. Hg. or more %
Non-Pregnant Controls.	74	21·6	61·4	17·0
6 Weeks before term TOTAL	174	37·4	40·2	22·4
MINUS COMPLICATIONS.	157	35·6	42·0	22·3
Weeks before term 1st	44	34·0	43·2	22·8
2nd	34	38·2	26·5	35·3
3rd	28	35·7	50·0	14·3
4th	32	37·5	34·4	28·1

The figures for Area "B" were similarly analysed and tabulated - Table XXI.

TABLE XXI.

AREA B	No	CRITICAL PRESSURE		
		150 mm. Hg. or less %	200 mm. Hg. %	250 mm. Hg. or more %
Non. Pregnant Controls	30	23·3	46·6	30
6 Weeks before term TOTAL	127	33	23·6	43·3
Weeks before term 1st	29	27·6	27·6	44·8
2nd	27	22·2	26·0	51·8
3rd	22	27·3	40·9	31·8
4th	22	45·5	9·0	45·5

From the foregoing Tables, it can be seen that there is a definite difference in the percentage distribution of tests when the expectant mothers' results are compared with those of the non-pregnant controls.

In Area "A", there is a very definite spreading of the distribution, cases "leaving" the 200 mm.Hg. group and going to both the lower and higher

pressure groups. The percentage incidence in the 200 mm.Hg. group being 61.4% in the case of the controls and only 40.2% when the findings for the last six weeks of pregnancy are taken as one group in the case of the pregnant women. Con-:versely, the incidence in the 150 mm.Hg. group rises from 21.6% to 37.4% and in the 250 mm.Hg. group from 17% to 22.4%.

The individual results for the 4 weeks just prior to term show a similar trend. They, in fact, indicate a significant fall in capillary resistance as term is reached. The percentage incidence in the 150 mm.Hg. group is approximately the same in all four ante-natal weeks which suggests that the changes take place before this period of gestation. The spread into the 250 mm. Hg. group is not, however, significant.

Area "B" results show also the spreading-out effect in the pregnant mothers as opposed to the controls, the incidence in the 200 mm.Hg. group being 23.6% in the former and 46.6% in the latter. The 150 mm.Hg. group rises from 23.3% to 33% and the 250 mm.Hg. group from 30% to 43.3%. There is, of course, a shift to the higher pressures in all cases because the normal values in Area "B" are higher than those in Area "A". It is noticed, however, that there is a greater tendency for cases to spread into the higher pressure group in Area "B" whereas the spread in Area "A" was more towards the lower pressure

group. Neither the 150 mm.Hg. nor the 250 mm.Hg. group Area "B" percentages differ significantly from the non-pregnant control group. This may be due to the smaller numbers of tests performed in this area.

For some unexplained reason, the third pre-natal week in both Areas "A" and "B" shows results closely approximating those of the non-pregnant controls. This may again be purely the effect, however, of paucity of numbers.

The effects of labour and the changes (if any) in capillary resistance during the puerperium of the 57 women were assessed in a similar manner. In Area "A" a further 267 natal and post-natal test results were added to the 174 ante-natal readings and these 441 results divided into the same three pressure groups as shown above. A composite Table showing the incidence ante-natally (during the last 6 weeks of pregnancy), during labour, and post-natally (during the 8 to 10 days' stay in hospital) was constructed. In Area "B" a further 238 test results were added and the total 365 results analysed and tabulated similarly (Table XXII).

Figure VI

C Control
AN Antenatal
N Natal
PN Postnatal

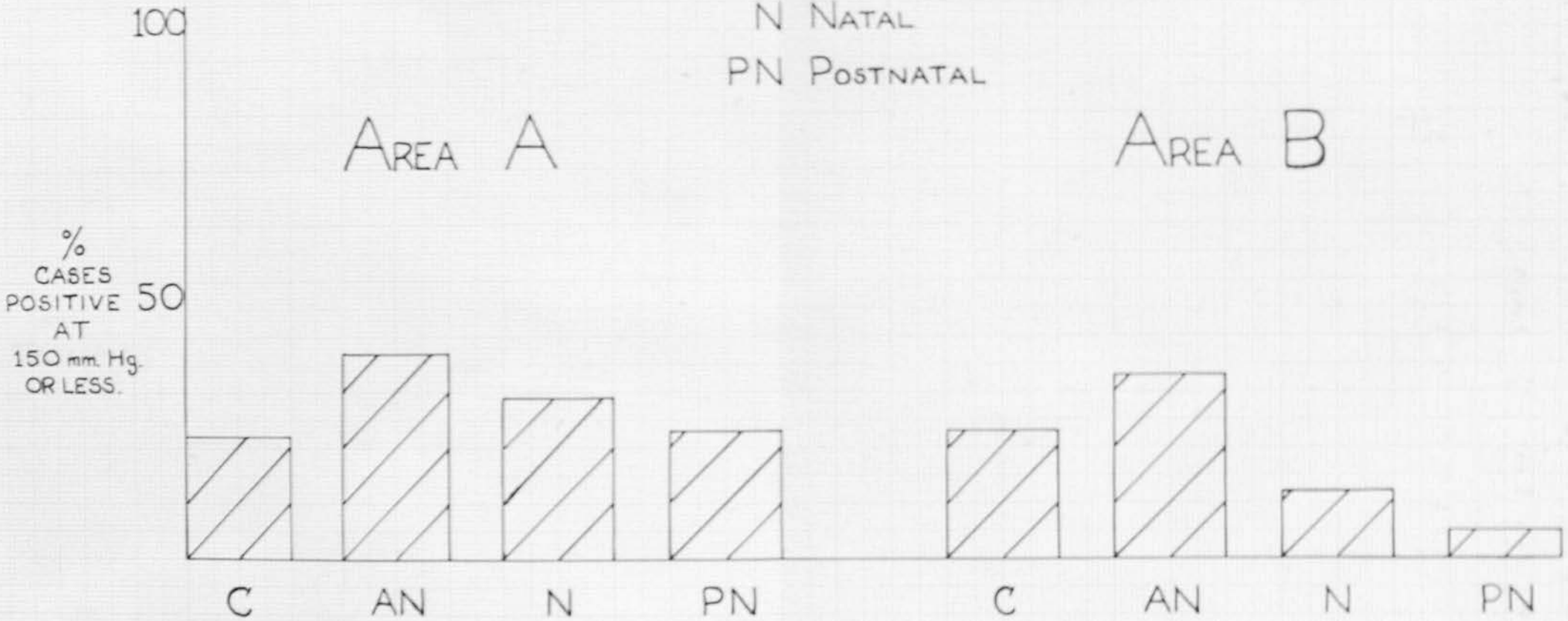


TABLE XXII.

AREA A		CRITICAL PRESSURE (mm. Hg.)					
		150 or less		200		250 or more	
		No	%	No	%	No	%
Non Pregnant Controls	74	16	21·6	45	61·4	13	17
Ante - Natal	174	65	37·4	70	40·2	39	22·4
Natal	83	24	28·9	29	35	30	36·1
Post - Natal	184	42	22·9	40	21·7	102	55·4
AREA B							
Non Pregnant Controls	30	7	23·3	14	46·6	9	30
Ante - Natal	127	42	33	30	23·6	55	43·3
Natal	68	8	11·8	18	26·5	42	61·7
Post - Natal	170	8	4·7	32	18·8	130	76·5

It can be clearly seen from Table XXII and Figure VI that both Areas "A" and "B" show a definite natal and post-natal shift towards the higher pressure groups, and that in the puerperal phase there are a great many more tests positive in the highest pressure group than are found among the non-pregnant control cases. The percentage incidence for example, in Area "A" 250 mm.Hg. pressure group, rises from 22.4% ante-natally to 36.1% during labour,

and to 55.4% during the puerperium, a significant change. This final percentage is significantly higher than the 17% of the non-pregnant controls. Exactly the same conclusions are deduced from the Area "B" findings.

An attempt was made to see at what point the maximum resistance was reached and daily analysis of the Area "A" puerperal tests was made (Table XXIII).

TABLE XXIII.

AREA A		CRITICAL PRESSURE (mm.Hg)					
		150 or Less		200		250 or more	
Time After Labour	Total Nos	No	%	No	%	No	%
Few Hours	17	5	29.5	4	23.5	8	47
1 day	33	8	24.2	8	24.2	17	51.5
2 days	18	2	11.1	5	27.8	11	61.1
3 .	22	7	31.8	3	13.6	12	54.5
4 .	24	4	16.6	6	25	14	58.4
5 .	11	2	18.2	3	27.3	6	54.5
6 .	23	9	39.1	3	13.1	11	47.8
7 .	17	1	5.9	1	5.9	15	88.2
8 .	13	4	30.8	4	30.8	5	38.4

Table XXIII shows no significant trend within the puerperium itself. The resistance would not appear to have begun to return to normal by the 8th day of puerperium as the percentage distribution up to this age is very similar to that obtained a few hours after labour.

A similar Table (Table XXIV) of Area "B" results was constructed to find, if possible, a turning point at which the capillary resistance begins to fall. This analysis was again necessary because of the differing response to negative pressure obtained on different areas of the body surface (Munro et al, 1947).

TABLE XXIV

AREA B		CRITICAL PRESSURE (mm. Hg.)					
		150 or less		200		250 or more	
Time After Labour	Nos	No	%	No	%	No	%
Few Hours	17	1	5·9	4	23·5	12	70·6
1 day	29	2	6·9	5	17·3	22	75·8
2 days	13	0	0	1	7·7	12	92·3
3 "	21	1	4·8	4	19	16	76·2
4 "	22	0	0	4	18·2	18	81·8
5 "	11	1	9·1	2	18·2	8	72·7
6 "	18	1	5·6	6	33·3	11	61·1
7 "	18	0	0	1	5·6	17	94·4
8 "	13	2	15·4	2	15·4	9	69·2

Unfortunately, the numbers are smaller than for Area "A", but it can again be seen that there is no definite shift to the lower pressure group as puerperium advances. As with Area "A", there is an isolated shift to the lower pressure on the 6th day, but this is not maintained. It can be said then that the return of capillary resistance to normal does not occur within the first week of the puerperium, thus supporting the views of Gianaroli (1945) and Minkowski and Venes (1948).

COMPLICATIONS IN PREGNANCY

It has been mentioned previously that certain mothers had antenatal and post-natal complications, but that the results from testing these patients were included in the analyses. Of the 12 pat-:ients whose course was not quite normal, 11 were tested and 4 (36%) showed a rise of capillary resistance of 100 mm.Hg. or more over the test period. Of the remaining 45 mothers in the investigation, 43 were tested and 22 (51%) showed a similar rise in resistance. Although there is an apparent difference between these two groups, the numbers in the former are too small to be of statistical value. Inspection of the individual results showed no other obvious difference between the findings in the "complicated" and the uncom-:plicated groups.

In order to make quite certain that the few mothers showing some complication of pregnancy were not putting a false complexion on the results, a further Table XXV was compiled omitting the tests done on these patients. Thus, 17 ante-natal and 8 intra-partum tests in Area "A" from one mother with mild pre-eclamptic toxaemia, local uterine infection and mastitis, two with mild hypertension (one of whom had local uterine sepsis in the puerperium), and one with a dis-:charging dental sinus were discarded. Likewise, the post-natal tests, 36 in all, from 2 further

cases of local uterine infection, 3 of mastitis, 1 each of aural polyp, puerperal convulsion (non-eclamptic) and phlebitis were also discarded. Comparing Table XXV with Tables XXII and XXIII it can be seen that the percentage spread ante-natally is practically the same in the whole group as compared with the "corrected" group. The increase in resistance during labour and the puerperium is almost identical in the two groups. It was, therefore, decided that as these "com-:plicated" cases did not alter the results in any way, they could be included in all the analyses.

These findings are in the main in agreement with those of Dieckmann et al (1948) who found that only 5% of 63 patients with pre-eclamptic toxaemia had an abnormal capillary resistance. They also found that of the 75 hypertensive patients only 14% had frankly abnormal capillary resistance, while another 22% had results which were considered as border-line.

TABLE XXV.

AREA A		CRITICAL PRESSURE (mm.Hg.)					
Ante-Natal (Weeks)	Nos	150 or less		200		250 or more	
		No	%	No	%	No	%
6	15	4	26·6	9	60	2	13·3
5	17	8	47	7	41·2	2	11·8
4	29	10	34·4	11	38	8	27·6
3	25	9	36	13	52	3	12
2	31	12	38·7	8	25·8	11	35·5
1	40	13	32·5	18	45	9	22·5
TOTAL	157	56	35·6	66	42	35	22·3
Natal	75	21	28	27	36	27	36
Post-Natal Few Hours	13	5	38·4	2	15·4	6	46·2
1 day	29	7	24·2	7	24·2	15	51·6
2 days	14	2	14·3	4	28·6	8	57·1
3 "	15	4	26·6	3	20	8	53·4
4 "	21	4	19	5	23·8	12	57·2
5 "	8	1	12·5	3	37·5	4	50
6 "	19	7	36·8	2	10·5	10	52·7
7 "	13	1	7·7	0	0	12	92·3
8 "	10	3	30	4	40	3	30
TOTAL	142	34	23·9	30	21·1	78	55

VITAMIN P AND MATERNAL CAPILLARY RESISTANCE

The literature concerning the effects of Vitamin P therapy on capillary resistance has been fully discussed in a previous section. Minkowski and Venes (1948) are the only workers found who gave a Vitamin P preparation to women during an uncomplicated pregnancy. They gave 40 - 100 mgm. of Esculoside during the early stages of labour and found that in "5 out of 10 cases the capillary resistance rose 100 points". Dieckmann et al (1949) on the other hand gave 20 mgm. of Rutin three times a day to 13 patients with so-called "abnormal capillary fragility" during the course of some pregnancy complication. They found that the resistance in 12 cases increased and in the 13th it diminished. It has been explained how 30 pregnant women were given this vitamin during the last 4 to 6 weeks of pregnancy and it now remains to compare their capillary tests with those of 27 controls not having the vitamin. Three patients in the Vitamin P group could not be tested at all and, therefore, there remain 27 patients in each group. Of the 27 in the Vitamin group a further 2 were tested in the puerperium only and 4 during labour and the puerperium only. Two control cases were tested ante-natally and post-natally, but were missed

during labour. The remainder of the two groups was tested during late pregnancy, labour and the puerperium. A total of 414 Area "A" and 365 Area "B" tests were performed.

The results are tabulated (Table XXVI) as before, and a comparison thus made between the vitamin and control groups for Area "A" and "B".

TABLE XXVI.

		CRITICAL PRESSURE (mm. Hg.)					
		150 or less		200		250 or more	
AREA A	Totals	No	%	No	%	No	%
Non Pregnant Controls	74	16	21·6	45	61·4	13	17
Ante-Natal Vitamin P	58	21	36·2	31	53·4	6	10·3
Controls	89	35	39·3	31	34·8	23	25·8
Natal Vitamin P	40	9	22·5	19	47·5	12	30
Controls	43	15	34·8	10	23·3	18	41·9
Post-Natal Vitamin P	89	22	24·7	14	15·7	53	59·5
Controls	95	20	21	26	27·4	49	51·6
AREA B Non-Pregnant Controls	30	7	23·3	14	46·6	9	30
Ante-Natal Vitamin P	50	19	38	13	26	18	36
Controls	77	23	30	17	22·7	37	48
Natal Vitamin P	31	6	19·4	7	22·6	18	58
Controls	37	2	5·4	11	29·7	24	64·9
Post-Natal Vitamin P	73	7	9·6	15	20·5	51	69·9
Controls	97	1	1	17	17·6	79	81·4

Table XXVI shows that Vitamin P does not appear to have any effect on the capillary resistance at any time during late pregnancy, labour and early puerperium. There is, in fact, a striking similarity between the two sets of results, the rise in both the vitamin and control groups being significant. It was for this reason that in the preceding sections the Vitamin P and control cases were considered as one group. It is possible that the obvious increase in capillary resistance obtained by Minkowski and Venes (1948) on giving the vitamin was, in fact, the rise obtained during normal labour and puerperium (see above) and that it was not due to the vitamin therapy.

Another method of assessing the effect of Vitamin P on the capillary resistance is to divide the cases into three groups; the first group consisting of all cases showing an appreciable rise in capillary resistance during the period of examination (i.e. 100 mm.Hg. or more); the second group consisting of all cases showing a fall of similar dimensions; and the third consisting of the cases showing no change at all or a rise or fall of only 50 mm.Hg. In each group, the Vitamin P and control cases were tabulated separately.

TABLE XXVII.

	CRITICAL PRESSURE TREND						
	RISE		FALL		NO CHANGE		
CASES	No	%	No	%	No	%	TOTAL
Vitamin P	10	37.1	1	3.7	16	59.2	27
Controls	16	59.2	3	11.1	8	29.7	27

It appears on examination of Table XXVII that the Vitamin P has had the effect of inhibiting the rise in capillary resistance obtained in the control group. 59.2% (16/27) of the Vitamin P cases showed no change in capillary resistance during the test period whereas only 29.7% (8/27) control cases showed no change. This change is not statistically significant, but the Table suggests that the vitamin did not increase the resistance in pregnant women, but on the contrary, tended to inhibit the normal increase. Whether it increases the resistance in the non-pregnant subject or in a person suffering from some pathological condition, as it is reputed to do, is quite another matter.

The mean initial resistance in the two groups is approximately the same so the apparent failure to rise of the cases in the Vitamin P group is not due to a higher initial resistance. It was considered justified in the light of these results to combine the groups for certain other analytical examinations.

CLINICAL COURSE IN RELATION TO MATERNAL CAPILLARY RESISTANCE AND VITAMIN P THERAPY.

The relation between Vitamin P and capillary function has been discussed above. It is not unreasonable to suggest that the vitamin may be related to haemorrhagic conditions, the type of "haemorrhage" in question at the moment being blood loss during labour and the duration of red lochia during the puerperium. The cases were, therefore, divided as in the previous section into those showing a rise in resistance (100 mm. Hg. or more), those a fall (100 mm.Hg.or more), and those showing an increase or decrease of resistance of 50 mm.Hg. or less. Though changes of 50 mm.Hg. may be of significance it was con-sidered that only changes of 100 mm.Hg. or more would be considered as important, thus increasing the accuracy of the observations. The 27 Vitamin and 27 control cases were divided into these three groups and further sub-divided into those showing normal, moderate or excessive blood loss at labour. They were also divided into those with red lochia of three plus days or less than three days' duration. (Table XXVIII).

TABLE XXVIII.

	CRITICAL PRESSURE TREND						
	RISE		FALL		NO CHANGE		
	P	C	P	C	P	C	TOTAL
LABOUR							
Blood Loss							
Normal	7	11	0	3	11	7	39
Moderate	2	5	1	0	2	1	11
Excessive	1	0	0	0	3	0	4
LOCHIA							
Duration (days)							
3+	7	10	0	2	9	5	33
2-	3	6	1	1	7	3	21

P = Vitamin P cases

C = Controls

Irrespective of the trend in the maternal resistance it can be seen that approximately the same number of Vitamin P cases (18) had a normal blood loss as did controls (21). The same relationship is maintained among the cases with moderate loss. It is interesting to note, however, that all 4 cases with excessive loss belonged to the vitamin group, and 3 of them showed "no change" in resistance. Although this suggests that a mother showing no change is more

likely to have excessive loss of blood at labour, the idea is not upheld in the group showing moderate loss. Here, 7 out of the 11 cases showed a rise in resistance; and it is noted that only 2 of them belonged to the vitamin group.

Twenty-three cases had red lochia of more than 3 days' duration, 17 controls and 16 vitamin cases. This again shows no over-all difference, but again it is noticed that only 7 out of 17 cases in the group showing a rise were Vitamin P cases. The same proportions exist, however, among the cases with red lochia for less than 3 days.

The Table, therefore, suggests that there is no relationship between a rise in resistance and the duration of red lochia. It also shows that there is no relation between capillary state and the amount of blood lost during labour. It suggests that the Vitamin P cases may have a tendency to greater loss than the controls. These findings, however, are not statistically significant and may well be due to chance variation. That no direct relationship has been shown is understandable when it is realised that this type of blood loss is not due to capillary haemorrhage alone.

CAPILLARY RESISTANCE AND TYPE OF LABOUR

It has been clearly shown by Robson (1949) and Scarborough (1948) that there is a definite capillary response to operation, the post-operative resistance being measurably greater than the pre-operative. Labour itself might be consider-:ed as a "physiological operation" involving tissue damage and blood loss and it has definitely been shown above that a rise in resistance occurs during, and after, labour. Two further points require clarification. Does obstetrical operative inter-:ference still further increase the capillary resistance ? And if it does, is this factor influencing the results of the group of tests as a whole ?

Table XXIX gives the comparison of cases entirely normal obstetrically with cases in which operative measures, including episiotomy, were required.

TABLE XXIX.

	CRITICAL PRESSURE TREND						
	RISE		FALL		NO CHANGE		
DELIVERY	P	C	P	C	P	C	TOTAL
Spontaneous	5	11	0	2	8	6	32
Operative	5	5	1	1	8	2	22
TOTALS	10	16	1	3	16	8	54

P = Vitamin P cases

C = controls

It can be seen that out of 32 spontaneous deliveries, 16 (50%) showed a rise in resistance. Out of 22 operative deliveries 10 (46%) showed a rise. The same close relationship between the two groups exists in the cases showing "no change" in resistance.

It can, therefore, be concluded that the effects of added obstetrical interference (if present) are not sufficient to enhance to any great extent the normal upward trend of resistance found in the patient delivering herself spontaneously. It seems unlikely, therefore, that the inclusion of these abnormal deliveries will invalidate the results. It is interesting to note that the only Caesarean Section delivery in the series showed literally no increase in resistance throughout the

test period; a case in which it would be reasonable to expect the resistance to rise.

Other factors than mode of delivery of the foetus and placenta must be concerned in the normal rise which occurs during parturition.

CAPILLARY RESISTANCE AND DURATION OF LABOUR

An attempt was next made to correlate the changes in resistance and the duration of labour. The question arises here, does prolonged stress during a long labour produce a proportional increase in capillary resistance ?

TABLE XXX.

	CRITICAL PRESSURE TREND					
	RISE		FALL		NO CHANGE	
DURATION of LABOUR	P	C	P	C	P	C
Less than 10 Hours	6	7	0	2	6	4
	13		2		10	
10 Hours or more	4	9	1	1	10	4
	13		2		14	
15 Hours or more	3	1	1	1	4	3
	4		2		7	

P = Vitamin P cases

C = controls

The approximate average duration of labour in the series was in the region of 11 hours, so the cases were divided into those whose labour was 10 or more hours long and those lasting less than 10 hours (Table XXX), the numbers in each group being 29 and 25 respectively. It can be seen at a glance that taking the vitamin and the control

cases as one group, there is no obvious tendency for the mothers with long labours to have higher critical pressures following labour.

Irrespective of the maternal resistance trend, it is seen that 15/29 (52%) of the women with long labours had Vitamin P. In the short labour group, 12/25 (48%) had the vitamin. This shows that the vitamin cases were evenely dis-:tributed between the two groups. The giving of the vitamin has not, therefore, influenced in any way the duration of labour. It has been shown in a previous section that Vitamin P appears to have "inhibited" the rise in capillary resistance seen in the control cases and it can now be said that this difference is not caused by a greater number of Vitamin P cases having short labours.

A further analysis of all cases with a labour lasting 15 hours or more was made in order to see whether these cases alone showed any significant change in resistance. There were 13 cases in all, 7 (54%) of which showed no change and 4 (31%) which showed a rise in resistance. These can be compared with 10/25 (40%) and 13/25 (52%) respectively in the short labour group. Here, although there is an apparent trend, owing to the lack of numbers it is not significant. There would appear to be a higher incidence of cases with long labours in the "no change" group and not, as was expected, in the "rising" resistance group.

CAPILLARY RESISTANCE AND GESTATION

Although every attempt is made to calculate gestation accurately, there is always the chance that the estimate may be a week or two inaccurate in either direction. The only way of obviating this difficulty is to examine very large numbers, and this was not possible in the present series. With this point in mind the cases were divided into Premature (39 weeks or less), Mature (40 weeks), and Post-mature (41 weeks or more). It is realised that some of the cases classified as Premature will, in fact, be Mature, but there were so few cases below 39 weeks' gestation that a separate group would have been of no value. There was only one case delivered at 35 weeks and one at 37 weeks, the remainder of the premature group being at 38 and 39 weeks. In the post-mature group there were two cases delivered at 42 weeks' gestation and the remainder at 41 weeks.

TABLE XXXI.

	CRITICAL PRESSURE TREND						
	RISE		FALL		NO CHANGE		
	No	%	No	%	No	%	TOTAL
Premature	8	42	1	5	10	53	19
Mature	10	50	2	10	8	40	20
Post-mature	8	53	1	7	6	40	15

Examination of the above Table shows at once that over the period 38 to 42 weeks there is no obvious change in capillary trend with increase in the period of gestation at which delivery occurs. The trends observed are therefore related to some change that occurs just prior to, during and after labour, irrespective of the duration of pregnancy.

SECTION III.

CORRELATION BETWEEN INFANT AND MATERNAL CAPILLARY RESISTANCE.

It only remains now to see whether or not there is any correlation between the infant and the maternal capillary resistance. First, the mother's capillary resistance in terms of mm.Hg. can be compared with that of the infant. Experience during this research has shown that the infant's initial capillary resistance when tested within 24 hours of birth can only be considered high if the test is positive at 150 mm.Hg. or more. After 24 hours, it can be considered high if positive at 200 mm.Hg. or more. The mothers' tests obtained early in labour, were divided into the usual three groups, 150 mm.Hg. or less, 200 mm.Hg., and 250 mm. Hg. or more. The findings in 49 mothers and their infants were thus tabulated (Table XXXII).

TABLE XXXII.

INFANT CRITICAL PRESSURE (mm.Hg)	MATERNAL CRITICAL PRESSURE (1st Stage Labour)					
	150 mm. Hg. or Less		200 mm. Hg.		250 mm. Hg. or more	
	Under 24 hrs	24 hrs and over	Under 24 hrs	24 hrs and over	Under 24 hrs	24 hrs and over
50	2	2	6	1	4	0
100	5	6	3	2	3	2
150	2	3	4	0	1	0
200	0	0	1	1	1	0

It can be seen from the above Table that of the 20 cases in which the maternal critical pressure was 150 mm.Hg. only 2 infants had initial pressures that can be considered high (i.e. 2/20 or 10%). In the 18 cases where the mothers' resistance was 200 mm.Hg., 6 can be considered high (i.e. 6/18 or 33%). Finally, in the highest group, 250 mm.Hg. and more only 2/11 or 18.2% are found to be high. Although it would appear in the lower two pressure groups that the infants' critical pressure rises as the mothers' pressure

rises, the third column does not uphold this finding. Owing to the lack of numbers the difference between the 10% in the 150 mm.Hg. group and the 33% in the 200 mm.Hg. group is not statistically significant.

The second method of assessing the correlation is to compare those mothers showing a definite rise or fall in resistance (100 mm.Hg. or more) and those showing a change of 50 mm.Hg. or less during the test period with the infants showing a rise, fall or no change in resistance.

It should be remembered that although 50 mm.Hg. change in critial pressure is not considered of importance in the mother it is considered so in the infant. "No change" in the infant tests means literally no change in critical pressure over the test period. The results from 53 mothers and babies were thus tabulated. (Table XXXIII)

TABLE XXXIII.

MATERNAL CRITICAL PRESSURE	RISE			FALL			NO CHANGE		
INFANT CRITICAL PRESSURE	R	F	NC	R	F	NC	R	F	NC
Number	21	3	2	3	1	0	16	5	2
Per cent	80·8	11·5	7·7	75	25	0	69·5	21·8	8·7

R = Rises
F = Falls
NC = No change

The Table above shows that the percentage of infants showing a rise is approximately the same no matter how the maternal capillaries are reacting to the effects of labour and the puer-:perium. At first glance these percentages would appear to indicate a trend. 80.2% of infants showed a rise in resistance when the mothers' resistance rose. For the "fall" and "no change" groups the percentages were 75.0% and 69.5% respectively. These differences did not, however, prove to be statistically signifi-:cant. This confirms the suggestion obtained from the above analysis that there is no absolute relationship between the infant and the maternal capillary resistance as tested by these methods. It is noted however that in most cases the resistance of mothers and infants rises from the time of birth till some time about or after the 8th day of the puerperium.

SECTION IV.

DISCUSSION.

It has been clearly shown in the above review of the literature on the subject of capillary resistance tests that even the minor differences in technique considerably alter the results. The site tested, time of exposure, magnification and illumination of the area vary from one worker to another. It is unfortunately impossible, therefore, to compare the present results, in terms of absolute values of mm.Hg. pressure, with pre-:vious reports.

It is not even known exactly what physiolo-:gical function or property of the capillary is being measured by this test. But that the results are consistent under standard conditions is con-:firmed. It is thus justifiable to express the "strength" of the capillary in terms of mm.Hg. No matter what technique is employed, therefore, provided the procedure is standardised throughout all the tests in any single series, trends in resistance observed by one worker may be compared with those obtained by another. The foregoing report of findings shows that in some respects they are at variance with those previously re-:ported; that some confirm previous work and that

the rest must remain in doubt until further re-
:search has been done.

The explanation of these capillary resistance trends in mothers and infants is difficult owing to the multipilcity of factors that might influ-
:ence the resistance over the period of time during which the tests were performed. These factors include the effects of circulating maternal sex hormones; the stress of labour and the possible adrenal response to this stress; the factor responsible for the "plethora visceralis" that is said to occur in the newborn at the ex-
:pense of its peripheral circulation (Smith, 1951); the sudden release of the hitherto constant surface pressure of the liquor amnii on the infants' skin and, therefore, on the cutaneous capillaries; and, probably, further as yet undiscovered facts concerning the vascular system of the newborn infant.

The first rather striking factor observed is that both the maternal and the infants' capillary resistance rose, in the majority of cases, from a definitely low value, from the time of birth onwards. This suggests that there is a factor influencing both mother and baby prior to labour and possibly persisting into the puerperium; a factor at the outset common to maternal and foetal circulations.

THE INFLUENCE OF MATERNAL SEX HORMONES.

The first common factor that suggests itself is the level of circulating OESTROGENS.

In the mother, there is a high concentration of oestrogens present at term (Kerr, 1944, Venning, 1948) and this falls away fairly rapidly. The exact time at which this fall occurs is not known, but Venning (1948) showed the excretion of oestrogen products to continue right up till the onset of labour and thus cast doubt on the previous suggestion that the fall occurred prior to its commencement. At the time when the concentration is at its height, the capillary resistance is lower than normal and as the concentration falls during labour and the puerperium the resistance rises. The rise observed is to levels far above normal and here the close inverse relationship is lost and a search for additional influences must be made. An interesting relevant fact, however, is that animal experiment has shown the administration of oestrogens to lower the resistance in dogs (Skelton et al, 1946) and it has been suggested that progesterone has the opposite effect (Loraine, 1952). Recently, Mauzey (1950), using the Venning method, has shown that pregnandiol excretion falls during the 17 days preceding labour. Twenty-four hours before parturition starts there is a rise and, although another fall is detected, considerable

quantities of pregnandiol are excreted throughout labour. Whether this accurately mirrors progesterone excretion is not fully established, but in the light of this the changes in capillary resistance evident during labour are not as likely to be related to progesterone as they are to oestrogens. However, a balanced effect may in fact occur.

If capillary resistance changes are related to sex hormone levels in the blood, one might expect changes during the menstrual cycle. These have, in fact, been observed and Brewer (1938) reported a transient lowering of resistance at mid-cycle and Venning (1948), using a bioassay method, found a brief rise in oestrogen excretion at approximately the same time. Brewer (1938) also found a fall in resistance prior to menstrual flow but this, according to Venning (1948) is about the time when a gradual fall in oestrogens was observed. The exact timing of Brewer's tests is not known and it could be that many of them were performed when the oestrogens were at their height about the 20th day of the cycle and not during the following 8 days when the fall occurs. Loraine (1952) suggests that the oestrogen fall occurs about 4 days before the menses flow and if this were the case Brewer's findings would fit this hypothesis more accurately still.

Accurate estimation of day-to-day fluctuation in oestrogen excretion during the menstrual cycle is not available. The methods of assay used so far

have been mainly biological and are inaccurate. Most workers agree however that a peak of total oestrogen excretion occurs about mid-cycle (12 - 15 days) and that there is a similar, though smaller, rise at about 21 - 24 days. Observations on the oestrogen excretion at the onset of menstruation are few and probably unreliable (Loraine, 1952). The inverse relationship is seen again, however, when the menses begin to flow - a rise in oestrogens coinciding with a fall in resistance. It must be remembered that this correlation is not an accurate one as two entirely different experiments are com-:pared, but the findings none-the-less give food for thought.

There is ample evidence to suggest that the newborn infant experiences the effects of change in concentration of sex hormone. Engorgement of the breasts, vaginal bleeding and changes in the os uteri, vaginal mucosa and prostate are said to be due to the withdrawal of oestrogens (Mitchell-Nelson, 1946). The effects of this withdrawal of hormone, obtained via the placenta, may be evident for several days after birth and it has been shown yet again that the capillary resistance rises throughout this period of fall in oestrogen concentration. There seems to be, therefore, a correlation between the concentration of oestrogen and the capillary resistance. If this were so, it would have to be concluded that in the pregnant woman and her infant an increase in circulating

oestrogen caused a fall in resistance. In the light of this it is a little surprising that a closer correlation between the mothers' and infants' resistance was not demonstrated. However, it has been shown that the response to administered oestrogens in different individuals may vary (Swyer, 1950) and this may also be the case with the naturally occurring hormone.

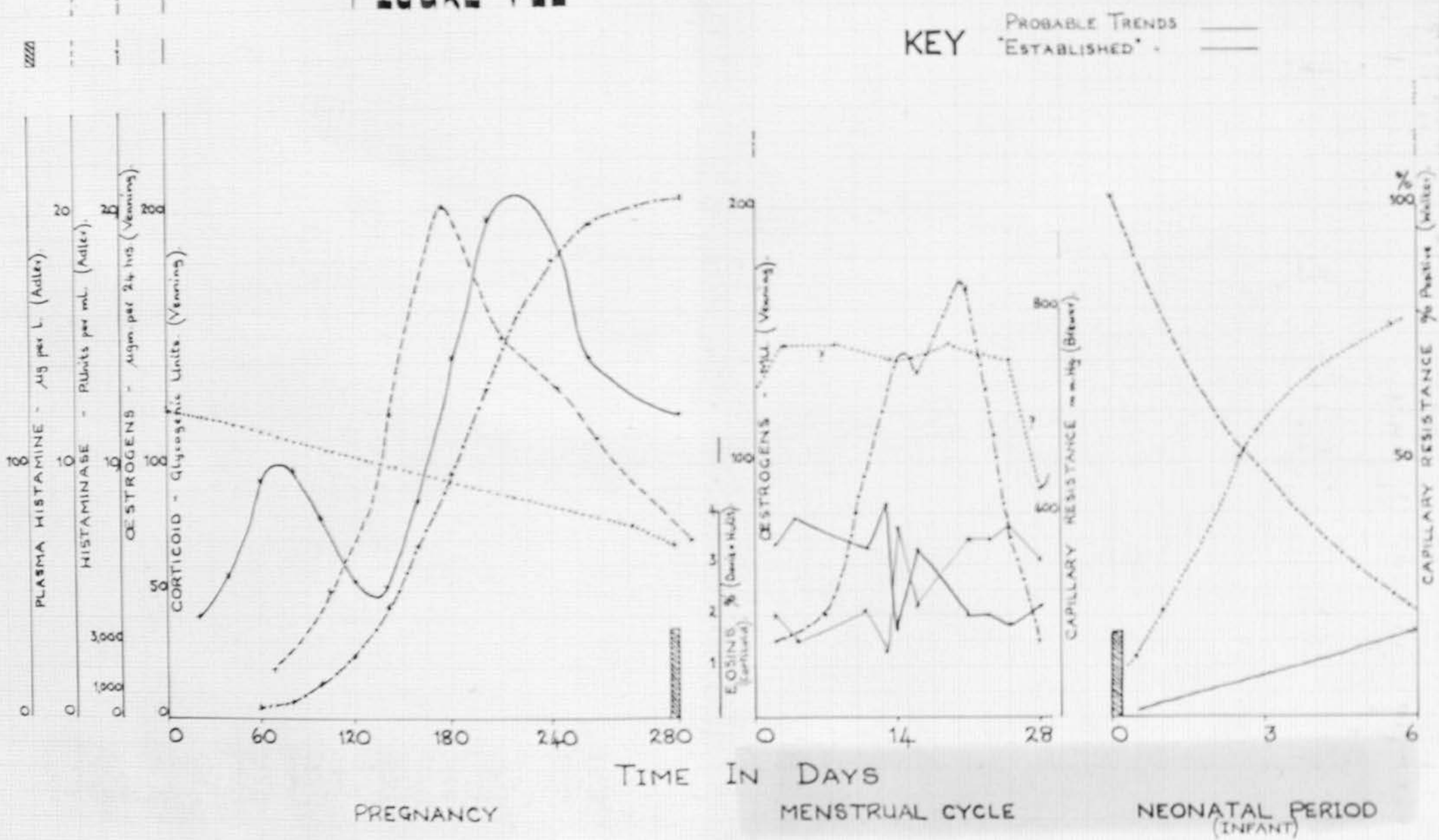
The whole subject of oestrogen estimation is at present in a state of flux. New and more accurate chemical assay is casting doubt on many of the previously accepted findings obtained by biological methods. It is, therefore, not possible, nor advisable, to be dogmatic about the exact timing of these changes in oestrogen concentration. It is likewise impossible to implicate any one of the three known human oestrogens - oestrone, oestriol and oestradiol or say whether it is the "combined" or "free" oestrogen that is the active principle. Oestriol is the most likely steroid responsible as nine-tenths of the oestrogens during pregnancy are of this type. It is thought that there is a fall in "combined" and a rise in "free" oestrogen at term which would suggest that it was an excess of the former type that caused the fall in capillary resistance. Doubt has recently been cast, however, concerning the existence of free oestrogen in vivo (Clayton and Marrian, 1950).

Another observation of note is that of Bean

et al (1949) who observed vascular spiders and palmar erythema from the 2nd to 5th month of pregnancy onwards. This would suggest an abnormal capillary function during this period when the resistance tends to fall and the authors attribute the changes they observed to exposure to high concentrations of oestrogens over a considerable length of time. Hertz et al (1949) administered very large doses of oestrogens to both males and females by intravenous injection and observed no vascular abnormalities whatever. This would suggest that it is not only the high concentration that is important but that it must be present for a considerable time before the capillary changes are manifest.

That there is a wide range of "normal" resistance (O'Hara and Hauck, 1936) has been confirmed by the present investigation and it is just possible that this range is due to differing levels of circulating hormone. This might also explain the different levels obtained on the same individual from time to time, bearing in mind that the male, as well as the female, is now considered to excrete oestrogens in the urine (Dingemanse et al, 1938). This does not account, however, for the tests performed on the one individual varying on the two arms. It is not unreasonable to suggest that this is due to additional local differences in vascular tone, skin texture and possibly temperature. It must also be remembered that several workers have

FIGURE VII


KEY
PROBABLE TRENDS
"ESTABLISHED"
PLASMA HISTAMINE - µg per L. (Adler)
HISTAMINASE - Units per ml. (Adler)
OESTROGENS - µgm per 24 hrs (Venning)
CORTICOID - Glycosuric Units (Venning)
OESTROGENS - m.u. (Venning)
EOSINS (Peripheral)
CAPILLARY RESISTANCE - m.m.Hg (Bibsey)
CAPILLARY RESISTANCE % Positive (Walker)
0
60
120
180
240
280
14
28
3
6
TIME IN DAYS
PREGNANCY
MENSTRUAL CYCLE
NEONATAL PERIOD
(INFANT)

observed a slow decrease in resistance with advancing age - and that this is accompanied by a withdrawal of hormone and not a rise as would be expected if oestrogens were the only influencing factor. Nor does this explanation account for the seasonal changes observed by many workers investigating adults and children, but this subject will be discussed in greater length below. It is less certain that there is a seasonal trend in the neonatal infant.

Although the sex hormone theory does not fulfil all the requirements and although some other factor, or factors, must also play a part in these variations, it is still possible that the menstrual, reproductive and neonatal trends could be caused by varying concentrations of blood oestrogens (Fig. VII). It is only at these times that sudden dramatic changes of concentration and resistance occur together in the normal healthy subject.

THE INFLUENCE OF THE ADRENAL GLAND

The next factor common to both mother and infant is STRESS. In the former, this is due to the active and prolonged effect of labour, and in the latter, to the trauma and anoxia of transit through the birth passages. These factors in themselves are not likely to alter capillary function other than possibly affecting local trauma

but the body responses which these stimuli evoke may well do. The response of the ADRENAL GLAND is one which may have some bearing on this subject.

It is well-known that when an individual, e.g. a woman in labour, is undergoing great muscular effort adrenaline from the Adrenal Medulla is secreted in large quantities. This has a peripheral vaso-constricting action and Robson and Duthie (1950) have shown that the resistance increases appreciably following the subcutaneous injection of adrenaline and they quoted several workers who obtained similar results. It is a little surprising to learn that at the time when generalised peripheral vaso-constriction occurs and the level of Epinephrine in the blood is high, i.e. prior to menstruation, there is a fall in resistance and that this fall is drama-:tic when the spasm is released and the menses begin to flow (Brewer, 1938). This latter phenomenon corresponds closely to the fall in resistance noted antenatally when peripheral vaso-dilatation has been observed (Burt, 1949). Once more, the situation is reversed for, during the puerperium, there is a definite rise in resistance which is not accompanied by vaso-constriction. In fact, the ante-natal vaso-dilatation is maintained well into the puerperium (Burt, 1949).

It has been suggested that a small blood loss during menstruation is related to a small fall in resistance (Brewer, 1938). In the light of the above, this might be put down to there being less

vaso-dilatation - in degree and/or duration. It is not unreasonable to expect the same circumstances to occur during labour, but in fact during these investigations no relationship between blood loss and resistance could be demonstrated. It is interesting to remember, however, that an increased bleeding tendency is often related clinically to low capillary resistance.

In the infant during the first 24 hours of life the vasomotor mechanism is extremely labile, the infant undergoing marked physiological changes which might have an effect on the peripheral circulation. No correlation could be found during this period between the resistance and the presence of erythema or cyanosis. The adrenal medulla of the newborn appears to provide little adrenaline compared with the adult gland, but it is suggested that paraganglial chromaffin tissue may supply an excess to offset this deficiency (Smith, 1951).

The subject of vasopressor substances during pregnancy and labour and their effect on the peripheral vascular system is not yet fully investigated and it would be unwise to form any opinion as to their effects on capillary resistance until more information becomes available. It can, however, be said that as far as one's knowledge goes, no relationship between capillary resistance and vasomotor function has yet been established in either mother or infant.

The adrenal cortex must also be considered as it has been recently suggested that the adrenocorticotrophic hormone (ACTH) of the anterior pituitary gland has an effect on capillary resistance. Robson and Duthie (1950) found a marked increase in resistance when giving ACTH to patients with rheumatoid arthritis and idiopathic thrombocytopenic purpura. Only one other similar report could be found, that of Bethnall et al (1951) who found a reversal of the Rumple-Leede test following ACTH therapy in cases of "hypersplenic syndrome". It is interesting to find that Cortisone prevented an increase in capillary permeability in allergic reactions (Selye, 1949) and it may, therefore, have an effect on the resistance (Ambrose and De Eds, 1947). No other published work could be found concerning the relationship between ACTH (and Cortisone) and the capillary resistance, but an impression obtained by Loraine (1952) while in the United States was that more recent unpublished work has not in every instance confirmed the findings described above. It is quite possible, however, that the maternal and infant adrenal response to stress during labour is related to their capillary resistance.

Although it is widely believed that almost all the actions of ACTH are performed by the liberation of either Cortisone (Compound E) or more probably Compund F it is not known whether they act on the capillary directly or antagonise

the other factors (toxines, antigens) which do so.

What evidence is there in the mother of adrenocortical activity and how do the capillaries behave in relation to this activity ? Venning (1948) using a bioassay method has discovered two peaks of corticoid excretion during pregnancy, one in the first and one in the third trimester. Tobian (1949) using a more accurate modified Loewenstein chemical assay confirms the finding that the quantity excreted in the third trimester is much greater than in the first, and states that the maternal adrenal cortex is hypertrophied in late pregnancy. Canton et al (1951) state that hypertrophy occurs in the pituitary and adrenal glands in "some" pregnancies. There is, however, a fall of corticoid output in the 10 weeks prior to labour (Venning, 1948) and some time during this period a slight but significant drop in capillary resistance occurs.

Additional evidence of corticoid activity during pregnancy is found in the peripheral blood picture. Hills et al (1948) showed that ACTH produced, in the presence of a normal adrenal gland, leucocytosis, lymphopenia and eosinopenia. This is precisely what happens during pregnancy and to a greater extent during labour (Rath et al, 1950). During labour, Davis and Hulit (1949) found the eosin count dropping to zero on occasions, but they do not agree with Rath et al (1950) as to when normal figures are regained, the former saying 3 days, and the latter 2 to 4 weeks.

It has been mentioned that the capillary resistance was found to fall before term when corticoid excretion was falling and when there is strong evidence to suggest high adrenal cortical activity during labour there is a marked rise in resistance. The rise continues well into the puerperium which coincides with the findings of Rath et al (1950) who consider the cortical effects to be evident for 2 to 4 weeks.

It is difficult to know just where operation and its effect on resistance fits into the picture. Tissue damage, blood loss, and a "stress" effect are common to both labour and operation. That a rise in resistance does occur in both is beyond doubt (Robson, 1949), but again one may have to look to the adrenal gland for the mechanism. It is interesting to find that during elective Cessarean Section (presumably prior to labour) similar adrenal responses to those found in normal labour were observed (Davis and Hulit, 1949).

The close relationship described above is not altogether upheld when the facts concerning the menstrual cycle are examined. Brewer (1938) noted a possible mid-cycle fall in resistance and Davis and Hulit (1949) found a slight eosinopenia at ovulation. This suggests that there was a fall in resistance at the time when adrenal activity was increased. The same relationship was observed just prior to menstrual flow.

The adrenal gland in the newborn infant is

proportionately very much larger than at any other time of life and this enlargement is almost entirely to do with the inner cortical zone (Venning, 1950, Mitchell-Nelson, 1946). This zona fasciculata, from which compunds E and F are probably liberated, undergoes involution immediately after birth by a process which is complete about the second week of life (Mitchell-Nelson, 1946). Despite this rather dramatic loss of tissue, there is a pro-:gressive increase in the activity of the gland from birth to an unknown age (Venning, 1950). It has been stated by Klein (1951) that the infant excretes higher quantities of neutral reducing steroids after one week of age that before.

Using eosinophil counts as a guide, Venning (1950) found the adrenal gland was more responsive to ACTH in the infant over one week old, and found the normal eosinophil count to rise at the end of the first day then fall to normal levels at 7 to 10 days. It is suggested that the high maternal ACTH levels inhibit the foetal pituitary gland and that at birth the effects of this ACTH wear off with a subsequent rise in eosinophil count during the first day. The infant pituitary then comes into its own and gradually takes over, the adrenal gland taking some 7 to 14 days to respond fully to this infant ACTH and this is reflected in a gradual fall in eosinophils. Jailer (1951) stat-:ed that the premature pituitary takes about 10 days to become active and respond to the adrenaline

test. All this makes up an attractice theory which will, of course, require further confirma-:tion. Clement Smith (1951) for example, quotes a wide range of normal eosinophil count in the newborn, and there will be no absolute proof that variations in the eosinophil count are an indica-:tion of ACTH activity till the latter can be estimated in blood.

One point is a little difficult to accept. If the infant adrenal has been stimulated by maternal ACTH sufficient to produce a low eosinophil count at birth, why does it take over a week before it responds to any great extent to injected ACTH ? It is understandable that the pituitary gland may take some days to become active, but the eosino-:penia would suggest adrenal activity. These blood changes must be due either to adequate infant adrenal function or, more likely, to the effects of maternal adrenal corticoids acting on the foetal haemopoietic system. The second suggestion is further supported when it is learned that the infant is 1 to 2 months old before the atypical electrolyte response to ACTH seen in the early days becomes similar to that of the older infant and child (Klein, 1951).

That the gland is stimulated by ACTH and is unable to respond is suggested by the presence of gross hyperplasia of the inner cortical zone. Analagous to the enlarged thyroid gland unable to respond to and, thereby, inhibit the secretion

of thyrotrophic hormone of the pituitary, the foetal adrenals may be incapable of response to relatively high concentrations of maternal ACTH.

It has been shown during this investigation that the capillary resistance of the newborn infant rises steadily from birth to an unknown age. The relationship between the resistance and the corticoid excretion is shown in Fig. VII. If the adrenal corticoids do increase the resistance, as has been suggested, this trend supports the idea but for one important factor. During the first 24 hours when the effects of maternal hormone are wearing off, a fall in resistance should be observed. That it was not seen might be explained by the timing and lack of sensitivity of the test, or that the resistance is a reflection of a delicate balance between the effects of corticoids and oestrogens on the capillary; the high concentration of oestrogens more than counteracting the less dramatic effects of maternal corticoids.

Some useful information regarding the factors influencing the capillary resistance of the newborn may be obtained by perusal of the findings in premature infants. Bayer (1930), Ylppö (1924) and Minkowski and Venes (1948) all agree that the more premature the infant is at birth the lower will be its capillary resistance. Lindquist (1937) and Bernfeld (1931) do not entirely agree, but the

findings in this investigation, without doubt, support this suggestion. Schwalm (1934) and Sanna (1934) found that the premature capillary took some weeks to develop fully and Eckstein (1933) showed that it expanded and contracted abnormally when exposed to temperature changes. It was noticed during this work also that the tendency to bruising and oedema was greater in the premature than in the mature infant. It is not unreasonable to suggest that the capillary resistance increases as the capillary develops, but it is possible that a different level of the vascular tree is being measured in the premature infant. Sanna (1934) is of the opinion that the finer capillary loops do not develop for some time and that it is the broader arches that are being tested.

From the point of view of circulating oestrogens it can be assumed that the concentra-:tion in mother and infant is lower at the time of premature labour than it is at full term. In the light of the above discussion one might then expect the premature infant to have a higher resistance than the mature, whereas the opposite is, in fact, the case. This lends weight to the suggestion that the difference in prematurity is due more to structural than hormonal factors. It is worth mentioning at this point that the pre-:mature infant of unspecified age responds very vigorously to ACTH therapy (Levine et al, 1951),

but that giving adrenaline produces a poor eosino-:phil response till about the 10th day (Jailer, 1951). It should be mentioned, however, that the adrenaline test is falling into disfavour as an assessment of adrenal function. The clinical res-:ponse on giving Cortisone to premature infants and observing their activity and appetite was consider-:ably less than that produced by ACTH (Levine et al, 1951) which might indicate a poor tissue response to Cortisone (Compound E) in the absence of the other adrenal corticoids.

Assuming, for the moment, that the foregoing hypothesis concerning the effects of Cortisone on capillary resistance is correct, and that the in-:creased adrenal corticoid secretion increases the resistance, the findings in premature infants fall into line. A poor adrenaline test response, poss-:ibly indicates a defective pituitary function, poor stimulation of the adrenal cortex, low corticoid secretion and, therefore, a lower capillary resist-:ance than in the mature infant. It must in fair-:ness be mentioned again, however, that even the mature infant has only a moderate response to ACTH injection on the second day of life which gradually improves during the following 10 days (Venning, 1950). The corticoid excretion in both the premature and the mature newborn is very low at birth and does not accurately reflect the level of maternal corticoid output prior to its birth.

There is a further point against the theory that the infant capillary resistance is influenced

by the level of maternal hormone. Assuming again that adrenal hormone increases resistance, and remembering that the premature infant has a lower resistance than the mature, a higher maternal corticoid output would be expected at term than prior to it. This is not, in fact, so. Venning (1948) showed that the highest output of corticoid occurred at about 30 weeks' gestation (Fig.VII), after which it fell till term when it was none-the-less still well above early pregnancy levels. Despite the high maternal ACTH the infant adrenal gland either seems unable to respond to it or the body response to Cortisone produced by it (maternal or foetal) is defective. Although no certain conclusion can be reached, it appears more likely that the low resistance in premature as compared to mature infants is due to structural rather than hormonal differences.

The functions of both the medulla and cortex of the adrenal gland in mother and infant have been discussed in some detail in order to establish, if possible, some relationship between them and the capillary resistance. Once again, as with the oestrogens, a close but not complete correlation has been shown. In the general picture of stress reaction, both medulla and cortex are said to play a part (Selye, 1950). The medulla and cortex need

not react to the same degree when exposed to the same stimulus, but it is a little surprising to find peripheral vaso-dilatation when the stress is at its height during late pregnancy, labour and early puerperium. In view of this incomplete relationship, it is unlikely that the capillary resistance is influenced by adrenal gland secre-:tions alone. It is of great interest that Venning (1946) has observed an apparent stimula-:tion of the adrenal gland on administering oestrogens and suggests that the high level of corticoid excretion in the third trimester of pregnancy may be "oestrogenic" in origin. The comparatively low oestrogen level in the first trimester could not, however, be responsible for the less dramatic rise in corticoid excretion at that time. Oestrogens and adrenal corticoids may, however, be closely related and may exert a combined effect on the capillaries.

THE INFLUENCE OF VITAMINS

The effects of VITAMIN P on the capillary resistance of the newborn and its mother have been studied, but unfortunately no definite conclusions have been reached. The fact that the resistance is not related to VITAMIN C concentrations alone is accepted fairly widely (Munro et al, 1947, Scar-borough and Bacharach, 1949) though there is still some doubt about the other factor related to resistance, "substance P" being a vitamin. The two substances are intimately linked, however, and

it is of great interest that Vitamin C is also closely associated with the adrenal cortex. That capillary resistance is altered when there is deficiency of Vitamin C and Vitamin P is beyond doubt, but it is not known whether the deficiency has a direct effect on the capillary wall or is operative via the adrenal hormones. That Vitamin C and adrenal cortical activity are closely linked is now widely accepted and Giroud (1940) showed that Vitamin C is required for adrenal corticoid synthesis. Ragan (1951) and Jailer (1951), however, doubt the fact. The adrenal gland has a higher concentration of Vitamin C than any other body tissue (Levine et al, 1951) and stress or trauma cause a reduction in this concentration with a fall in blood and urinary levels of Vitamin C and a rise in urinary corticoids. ACTH on the other hand produces a rise in blood and urine Vitamin C as well as increased urinary corticoids (Beck et al, 1951). ACTH and Cortisone appear to ameliorate scurvy symptoms (Ragan, 1951, Schaffenberg et al, 1950), but the latter is not apparently able to replace Vitamin C entirely in the treatment of scurvy. It does, however, counter the high cortical activity found in this condition in guinea-pigs (Clayton and Prunty, 1951). Although the exact relationship is by no means clear, these authors, in the light of a comprehensive review of the literature and in the light of their own work, conclude that the balance of evidence is in

favour of there being increased adrenal cortical activity in scurvy. This suggests that the adrenal gland responds to the Vitamin C deficiency state by secreting excess hormone and thus attempts, among other things, to restore the low capillary resistance to normal.

That the resistance trend in the newborn infant has no relation to Vitamin C concentrations in the blood per se is suggested by two observa-:tions. First, the foetus and infant have been shown to have as high, or higher, levels of Vitamin C in the circulation as the healthy mother (Lund and Kimble, 1943, Slobody et al, 1947); and second, there is a fall in this level to normal at about 72 hours of age. If the resistance was related to the vitamin concentra-:tion alone, no change or a fall in the former might be expected at this time, whereas in fact a rise occurs, the infant's resistance being at its lowest when the vitamin concentration is at its highest. It is suggested that the maternal ACTH level is high at term and Beck et al (1951) have stated that ACTH increases the infant's blood Vitamin C level. This might be the explana-:tion of the high neonatal blood concentration, but the fact that it is sometimes higher than that of the mother indicates either selective retention of the vitamin as suggested by Lund and Kimble (1943) or some other specific unknown response, possibly adrenal, to the maternal hormone.

It is worth mentioning another entirely different observation at this point. Vitamin C

deficient guinea-pigs with a low resistance show a rise when given Para-aminobenzoic Acid (PAB) and that this effect can be offset by giving a drug of the sulphonamide group, Para-aminophenyl sulphamide (Parrot and Cotereau, 1949). It was, therefore, suggested that PAB might be concerned in the control of capillary resistance. The antagonism between PAB and the sulphonamides is recognised and the sub-:strate competition regarding the survival or death of organisms is well-known. It is also accepted that during infections the capillary resistance falls and the body requirement of Vitamin C increases.

It has, therefore, been suggested that the sequence of events is as follows : (1) invasion of the body by an organism; (2) the using up of PAB by the organism; (3) subsequent increase in utilisation of Vitamin C; (4) a fall in capillary resistance; (5) the need of increased Vitamin C intake. The giving of Vitamin P is said to assist the storage of, and/or aids Vitamin C in some unknown way in the control of the capillaries (Cotereau et al, 1948: Munro et al, 1947). This appears to be an attractive hypothesis, but one which is founded on rather doubtful evidence. There is no doubt, however, that the resistance is lowered in many clinical conditions, not the least of these being bacterial infection and vitamin deficiency disease. What part the adrenal gland plays in such conditions remains a matter of speculation.

There is some evidence to suggest that the seasonal variations in resistance are related to

fluctuation in the intake of Vitamins C and P containing foods. It might be expected that during the winter and spring months when fruit and vegetables are scarce and expensive, a deficiency might be reflected in the state of the capillaries (Gothlin, 1931). There is, however, some slight disagreement in the literature as to the actual months at which the resistance is at its lowest. The seasonal availability of fruit and vegetables varies from one country to the other and if the seasonal trend were related to their intake one might expect reports from various parts of the world to differ.

Before dismissing the subject of seasonal variations a detailed report by Biskind (1946) is worthy of note. There appears to be ample experimental evidence to suggest that oestrogens are inactivated by the liver and that under-nutrition, particularly involving the Vitamin B group, causes sufficient liver damage to depress this process of inactivation. Oestrogens normally inactivated by the liver therefore accumulate in the body and could cause an alteration in the capillary resistance. This under-nutrition, possibly seasonal in time, might well include lack of Vitamin C, but this idea once more indicates how closely related all these factors are to capillary resistance. No final conclusion on these points can, however, be reached.

THE INFLUENCE OF ANOXIA, HISTAMINE AND THE AMNIOTIC FLUID.

A further factor which might influence the infant and its capillaries is ANOXIA. It has been shown that oxygen saturations of 15% to 25% effect an increase in capillary permeability (Henry et al, 1947) and that up to one in six normal infants have such saturations (Clement Smith, 1951). Although permeability and resistance are quite separate entities, it has been shown that there is a close relationship between them and the suggestion arises as to whether or not states of anoxia alter capillary resistance. A distinction must, of course, be made between the spontaneous production of petechiae (caused by increased venous pressure during birth) often seen on the forehead and face, and actual lowering of resistance due to anoxia per se. The results of the present experiments do not support the suggestion that anoxia (as judged by peripheral cyanosis) influences the resistance in any way. It should be remembered, however, that cyanosis of the extremities was not always accompanied by cyanosis of the test area on the back. That some anoxia was present is a possibility, but it would certainly not be of the same degree. The newborn infant is particularly able to withstand states of anoxia and it does not seem likely that the common minor degrees of oxygen desaturation

per se will have a detectable effect on peripheral capillary resistance of the newborn.

Although it seems unlikely that anoxia per se has any direct effect on capillary resistance, it may well do through the medium of HISTAMINE. The first point of importance is the observation of Robson and Duthie (1950) that intravenous infusion of histamine caused a definite fall in capillary resistance and two other workers were quoted as having obtained similar results.

A finding which suggests that histamine might have a rather unusual effect on certain blood vessels in the newborn is that of Rogers (1950). He showed that the umbilical arteries were very sensi-:tive to minute amounts of histamine which caused an irreversible spasm, and suggests this as one mechanism of closure of these vessels. It is difficult to understand why this should occur when the typical response to histamine in man is one of arteriolar dilatation and capillary paralysis (The Triple Response).

The important relationship between histamine and anoxia has been reported by Graf (1949) who observed high blood histamine concentrations in cyanosing congenital heart lesions and in mice undergoing slow suffocation. This is due to the fact that histaminase is inactive in the absence of oxygen thus allowing accumulation of histamine (Kapeller-Adler, 1952). Pettay (1950) quotes

several authors as stating that the histamine content of animal tissues increases during birth - when a degree of anoxia usually occurs. His own work showed that the histamine concentration of umbilical cord plasma is two or three times greater than normal adult plasma.

Kapeller-Adler (1952) tested both mothers and infants and found approximately the same amount of histamine in the maternal and cord plasmas and a higher cell content in the cord blood at the time of delivery. More important, however, was her finding that while the mothers' plasma contained considerable quantities of histaminase, none could be detected in the cord plasma. This is similar to the findings of Swanberg (1949) who showed the "histaminolytic action" of umbilical blood to be one hundredth to one thousandth of the maternal blood ... thus approximating to those found in adult males and non-pregnant females.

In the infant, therefore, where the effects of trauma and anoxia are present together, the cord blood shows a high histamine content. There is little or no histaminase to destroy this and it is therefore free to exert an effect on the capillaries. As might be expected, a low capillary resistance is observed immediately after birth.

In view of the effect of anoxia on the blood concentration of histamine and thus on the capillary resistance, it is perhaps a little surprising that the cases showing peripheral cyanosis did not

show a lower resistance than the controls. This again may be due to the sensitivity of the test being insufficient to detect small changes of resistance or to the anoxia being of such a degree that only a small quantity of histaminase was inactivated.

In the mother during uncomplicated pregnancy the reaction to histamine injection is abnormal (Roberts et al, 1944) and it has been shown that maternal blood contains considerably more histaminase than the non-pregnant subject (Kapeller-Adler, 1951). This is apparently produced by the decidual portion of the placenta (Anrep et al, 1947, Swanberg, 1949) and Swanberg found a peak at the 22nd - 26th week. There is a gradual fall till early pregnancy levels are reached about the 4th day of the puerperium (Fig. VII). This does not entirely agree with the results obtained by Anrep et al (1947) who found the maximum concentration at term, but there is little doubt that histaminolytic substances are present at term in considerable concentration.

At term therefore both histaminase and histamine are detected in maternal plasma, the former in considerable quantity. It is perhaps less likely therefore that the capillary function in the mother is affected by this histamine, but its presence coincides with the prenatal fall in resistance. As labour and puerperium progress the histaminase concentration falls and theoretically

the histamine (if still present) should be free to produce a further fall in resistance. At this time, however, a rise in resistance occurs.

The exact timing of the disappearance of the histaminase is still rather in doubt. Kapeller-Adler (1951) finds normal levels are reached about the 4th day whereas Anrep et al (1947) obtained these about 48 hours after labour. This may be due to differences of experimental technique, but it can be said that this histaminase returns to non-pregnancy levels as the capillary resistance is rising.

In view of these facts it is possible that histamine plays a part in the control of capillary resistance in the mother and her newborn infant. The absence of histaminase in umbilical cord plasma and the fact that the newborn infant has been exposed to both trauma and anoxia make this poss-:ibility more likely in the case of the infant than of the mother.

As it is not possible to estimate the capillary resistance by the described method before and after the pressure effects of the AMNIOTIC FLUID have been released, no findings about this factor can be discussed. Sudden release of this over-all pressure might allow a flooding of the peripher-:al circulation. This would show itself as vaso-dilatation, fall in blood pressure and probably visible erythema. The latter does at times occur

for one reason or another, but is not a constant finding and does not appear to bear any relation to resistance. It appears that other body mechanisms for maintaining an adequate visceral blood supply offset this theoretical tendency to peripheral flooding.

In the light of the foregoing paragraphs it is interesting to note that a very high histaminase concentration has been observed in the liquor amnii (Swanberg, 1949). It is possible that this exerts an effect when applied to the surface of the skin for a long period of time though this is unlikely to be the whole story. The fact that it is present in such high concentration is likely to be of considerable importance, but once more the full significance of these findings and their effect on capillary resistance remains obscure.

CONCLUSION

It can be seen that it is impossible to implicate any one of the above factors as being responsible for the changes in capillary resistance in mothers and their newborn infants. It is probable that the structural development of the capillary is primarily important and that this is reflected in the definite changes in resistance that occur relative to prematurity and birth weight. Seasonal changes in resistance

are not observed in newborn infants and those seen in children and adults are possibly related to under-nutrition, with particular regard to Vitamins C and P and to liver dysfunction. It is quite likely that a number of factors work together to effect the other changes detailed above and that the most notable are probably the circulating oestrogens, the adrenal cortical hormones and histamine in that order.

SUMMARY

SECTION I

1. A total of 3,173 capillary resistance tests were performed on 1,268 occasions in 675 cases. Of these, 1,735 were done on 518 newborn infants, 1,276 on 83 mothers or expectant mothers, and 162 on 74 non-pregnant nurse controls.

2. The methods of testing capillary resistance in infants and adults used by previous workers are reviewed and reasons given for the technique adopted during the present investi-:gation. The importance of some minor de-:tails concerning apparatus and procedure is demonstrated. A direct relationship between bruising and oedema and the number of petechiae produced was observed. A relationship be-:tween the results obtained with a 1 cm. and a 2 cm. suction cup was obtained.

3. An attempt was made to demonstrate the presence or absence of a seasonal change in resistance. Although the percentage incidence at 150 mm.Hg. in infants aged 1 - 4 days appeared higher in the months May - June compared to September - October this was an isolated finding. No over-all trend for the

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whole year could be demonstrated. The incidence in infants up to 24 hours of age, on the other hand, was highest in the months July - August.

4. In only 9% of cases of intracranial haemorrhage of all kinds could a seasonal variation be shown. These were all stillborn infants who had sub-arachnoid or intra-ventricular haemorrhage. The incidence was highest in the second quarter of the year coinciding with the time at which infants aged 1 - 4 days appear to have a lower capillary resistance. This does not, however, coincide with the trend in infants up to 24 hours of age.

5. There is a significant increase of resistance from birth, when it is at its lowest, till the end of the first week of life - the end of the period of observation.

6. Premature infants have a lower initial resistance, but show a simlar increase with advancing age.

7. The resistance would appear to vary according to birth weight even within the mature weight group. The greater the weight at birth the greater the initial resistance.

8. There is no difference in capillary resist-:ance between the male and the female infant.

9. Investigating the effects of Vitamin P on the infant when given to the mother ante-natally gave an inconclusive result. The vitamin appeared to strengthen the capillaries to a very slight degree. Statistical proof is lacking.

10. The mode of delivery, the giving of Vitamin K, and the presence or absence of jaundice did not appear to influence the resistance.

11. The presence or absence of cyanosis of the extremities did not appear to be related to the degree of capillary resistance.

SECTION II

12. Normal adult female variation in capillary resistance is discussed and methods of test-:ing fragility reviewed.

13. The capillary resistance findings in pregnancy, labour, and puerperium are reviewed and in-:vestigated. There is a significant fall in resistance prior to term comparing the pregnant women with non-pregnant controls. A signi-:ficant rise in resistance during labour and

the puerperium is demonstrated, the final resistance being significantly higher than the non-pregnant control group. This de-:monstrates an "over-compensation" effect following the onset of parturition.

14. The minor complications of pregnancy en-:countered did not appear to alter these trends.

15. The effects of Vitamin P on the pregnant woman were studied and the analyses of re-:sults were inconclusive. The analysis of absolute values showed no differance between the vitamin and the control group.

16. There appears to be no relationship between the capillary resistance and (a) the dura-:tion of red lochia after labour, and (b) the amount of blood lost during labour. The Vitamin P cases tended in this series to have greater blood loss than the controls, but it must be remembered that this is not a measure of capillary haemorrhage.

17. Obstetrical operative procedure did not alter the resistance trends to any detectable degree. Maternal capillary resistance does not appear to be related to the period of gestation at which labour occurs or to the

duration of labour itself.

SECTION III

18. There is apparently no relationship, either in the absolute values or the trends, between the infant and the maternal capillary resist-:ance, but in most cases the maternal and infant resistance rises from the time of birth till about or after the 8th day of the puerperium.

SECTION IV

19. The literature concerning each of the fore-:going aspects of this subject has been reviewed. In the light of this information the possible causes of the findings in this investigation have been discussed.

20. No single factor could be considered as the influence initiating the capillary resistance changes observed. It was concluded that the resistance was probably controlled by a bal-:ance of several factors, notably oestrogens, adrenal cortical hormones, histamine and vitamin deficiency.

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